Draft Comparative Effectiveness Review

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Labor Dystocia

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Purpose of Review

To review the evidence on the definition of "normal" labor progression, and the comparative effectiveness of different strategies for treating labor dystocia in women with otherwise uncomplicated pregnancies. Strategies assessed include amniotomy, supportive care measures, epidural analgesia, frequency of cervical examination, intrauterine pressure catheters, high- versus low-dose oxytocin protocols, electronic fetal monitoring or intermittent auscultation during augmentation with oxytocin, and delayed or Valsalva pushing.

Key Messages

- Modern labor curves constructed from the Consortium on Safe Labor demonstrate that "normal" labor is significantly longer in nulliparous women compared to parous women.
- Older maternal age is associated with a longer first stage of labor among nulliparous women, and longer second stage of labor in both nulliparous and parous women.
- These modern labor curves suggest a longer "normal" duration of the first stage of labor, although the high prevalence of augmentation in these data prevent drawing inferences about the duration of normal labor in the absence of interventions.
- Use of partograms did not impact important maternal or neonatal outcomes.
- Amniotomy is likely to decrease the total duration of labor in nulliparous women with no differences in adverse outcomes.
- Amniotomy plus oxytocin decreases duration of labor without increasing cesarean delivery rates in both nulliparous and parous women.
- Emotional support interventions may reduce cesarean deliveries and instrumental deliveries.
- For women choosing analgesia, type (epidural vs. combined spinal epidural, or epidural versus patient-controlled intravenous analgesia) or timing during labor is likely to not affect cesarean delivery rates.
- Higher doses of oxytocin augmentation are likely to result in lower cesarean delivery rates compared to low-dose protocols, but cesarean rates may not be affected by timing in labor or by pulsatile versus continuous administration.

This report is based on research conducted by an Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. xxx-xxxx-xxxxx). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may periodically be assessed for the currency of conclusions. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at www.effectivehealthcare.ahrq.gov. Search on the title of the report.

Persons using assistive technology may not be able to fully access information in this report. For assistance contact EffectiveHealthCare@ahrq.hhs.gov.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Labor Dystocia

Structured Abstract

Objectives: This review evaluates the comparative effectiveness of different strategies for treating labor dystocia (difficult or obstructed labor) in women with otherwise uncomplicated pregnancies.

Data Sources: We searched PubMed®, Embase®, CINAHL®, and the Cochrane Database of Systematic Reviews (CDSR), limiting the searches to studies in the English-language and comparative studies published from January 1, 2005, to January 2016.

Review Methods: Two investigators screened each abstract and full-text article for inclusion, abstracted data, rated quality and applicability, and graded evidence. When possible, random-effects models were used to compute summary estimates of effects.

Results: Our review identified 111 articles (105 unique studies). This included 12 studies relevant to defining abnormal labor, eight studies about amniotomy, 50 studies on supportive care measures, 22 studies regarding epidural analgesia, one study regarding cervical examination, 1 study relevant to intrauterine pressure catheters, 12 studies relevant to high-dose versus low-dose oxytocin protocols, no studies on fetal monitoring strategies, and 2 studies of timing of pushing in the second stage. Evidence suggests that the duration and pattern of "normal" labor progress based on modern management is quite different than historical data, and that labor progress is longer in nulliparous compared to parous women. Use of partograms (graphs of cervical dilation versus time) did not impact important maternal or neonatal outcomes, although the applicability of this evidence to modern U.S. settings is limited. Routine amniotomy decreases the total duration of labor in nulliparous women without affecting other outcomes (moderate SOE), while routine amniotomy with oxytocin augmentation as needed decreased duration of labor without increasing cesarean delivery (high SOE). Although supportive care therapies are often seen as benefiting parental satisfaction with the birthing process, these outcomes were rarely assessed in clinical trials. However, an existing systematic review of 11 studies did find that women receiving continuous emotional support were less likely to rate their birth experience negatively (moderate SOE). Of the different types of supportive therapies, only emotional support interventions showed reductions in cesarean (low SOE for doula support, moderate SOE for continuous emotional support) and instrumental deliveries (moderate SOE). For women choosing analgesia, type (epidural vs. combined spinal epidural, or epidural vs. patient-controlled intravenous analgesia) or timing during labor did not affect cesarean delivery rates (moderate SOE).

Conclusions: Dystocia is a common indication for cesarean delivery. Recent data demonstrate that the normal progress of labor with current practice is quite different from curves originally described, although there is still uncertainty about the duration of "normal" labor in the absence of augmentation. Amniotomy and oxytocin decrease duration of labor without increasing cesarean delivery. Emotional support reduces operative delivery rates and patient satisfaction. Further work is needed to identify strategies for management of labor that optimize maternal and neonatal outcomes and patient preferences while minimizing cesarean delivery rates.

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Background

Condition and Treatment Strategies

Approximately 80 percent of American women will eventually have at least one child,[1] and the majority of these women will undergo labor. "Labor dystocia" (difficult or obstructed labor)[2] encompasses a variety of concepts, ranging from "abnormally" slow dilation of the cervix or descent of the fetus during active labor[3] to entrapment of the fetal shoulders after delivery of the head ("shoulder dystocia," an obstetric emergency). For the purposes of this systematic review, we assume that "labor dystocia" refers to "abnormal" labor progression during the latent (up to 4-6 cm dilation) or active phases (from 4-6 cm until full dilation) of the first stage of labor, or during the second stage (from complete cervical dilation until delivery of the baby). We also limit our review to women in spontaneous labor and exclude those who are undergoing induced labor.

Prolonged labor may increase the risk for maternal and neonatal infection, fetal distress, neonatal hypoxia, uterine rupture, and postpartum hemorrhage; it may also be a marker for increased risk of maternal pelvic floor and genital trauma during delivery (with a subsequent increased risk for future incontinence and pelvic organ prolapse) and of shoulder dystocia. Reducing the likelihood of these adverse maternal and neonatal outcomes is the underlying rationale for performing a cesarean delivery for the primary indication of labor dystocia.

However, there is a tradeoff, since cesarean delivery itself increases the risk of maternal hemorrhage, venous thromboembolism, and injury to the bladder and other internal organs, and can affect post-delivery mother–baby interactions. Further, having one cesarean delivery increases the likelihood of having subsequent cesarean deliveries.[3] A woman's risk for abnormal placentation (placenta previa or accreta, each of which is associated with significant maternal and neonatal morbidity and mortality) is directly related to the number of prior cesarean deliveries she has had.[4]

Although there is no consensus on the "optimal" cesarean delivery rate (conceptually, the rate that strikes a balance between benefits and harms for both mother and baby that is considered acceptable to most patients), there is widespread consensus that current rates in the United States are too high.[3,5] Strategies to prevent a woman's first, or primary, caesarean delivery may therefore lead to significant improvements in maternal and neonatal outcomes by reducing both the number of primary and repeat cesareans.[3] For this reason, the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) have issued a joint consensus statement aimed at "preventing the first cesarean delivery."[3] Strategies aimed at reducing cesarean delivery for dystocia are a key part of this, since abnormalities of labor progression are the single most common cause of primary cesarean delivery in the United States, accounting for over a third of procedures.[6]

The effective management of labor dystocia is first dependent on the tool used to diagnose the disorder. In the 1950s, Friedman published his observations on the rate of cervical change among a cohort of women in spontaneous labor[7] and from this constructed labor curves representing the expected rate of cervical change in a population. Deviations from these curves, particularly rates of cervical change slower than expected from the Friedman curve are referred to as protracted or arrest disorders and represent labor dystocia. The Friedman curve has been the

primary tool used to diagnose abnormal labor since then, though more recent data from the Consortium on Safe Labor have demonstrated that rates and characteristics of cervical change seen in modern obstetrics are quite different from that represented by the Friedman curve.[8] Identifying what constitutes normal labor is an important initial step in the management of labor dystocia as it first dictates when various treatment options are initiated.

After labor dystocia has been diagnosed, there are a number of strategies for treating abnormal labor that are addressed in this report:

- Use of graphs of cervical dilation versus time ("partograms") to identify patients with slow labor progress, often with an indicator of when intervention is appropriate
- Timing of the artificial rupture of the amniotic membranes (amniotomy) during labor
- Various options for maternal positioning, ambulation, and feeding during labor
- Use of epidural analgesia, or, alternatively, variations in technique (timing, choice of analgesic agents)
- Variations in monitoring labor progress (such as frequency of cervical examination or use of intrauterine pressure catheters) and fetal well-being (fetal heart rate monitoring)
- Variations in strategies for how oxytocin is used during labor augmentation including timing of augmentation relative to labor progress and variation in dosing regimens used
- Variations in strategies for reducing the length of the second stage of labor (after cervical dilation is complete but before the baby has delivered), including different approaches to maternal pushing

The overall goal of treating labor dystocia is to optimize delivery outcomes for mother and child, while attempting to achieve an optimal cesarean delivery rate. As discussed above, the optimal cesarean delivery rate is not known but is the lowest rate that balances benefits and harms to mother and child.

Scope and Key Questions

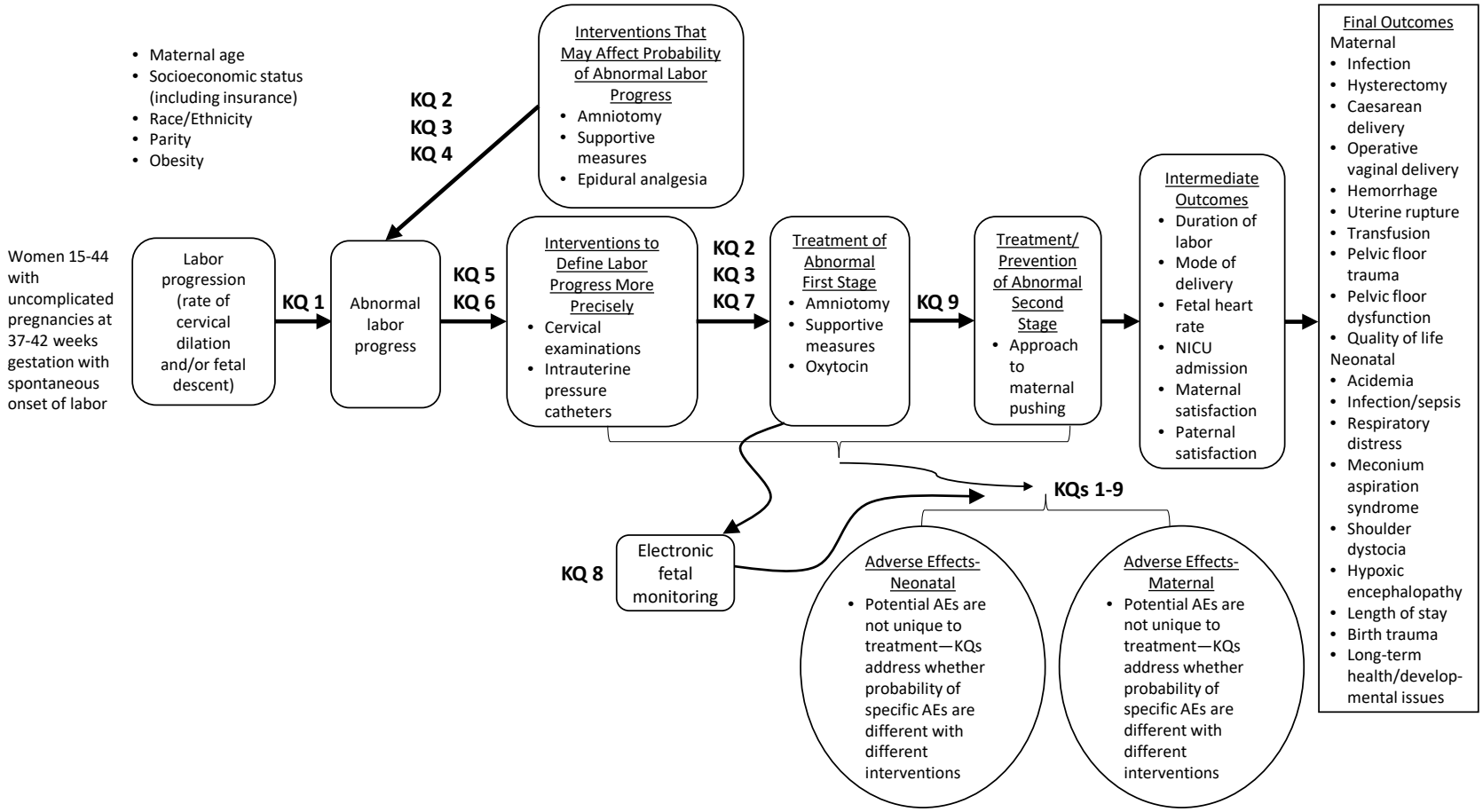
This systematic review evaluates the comparative effectiveness of different strategies for treating labor dystocia in women with otherwise uncomplicated pregnancies. In addition, one potential source of uncertainty in the available evidence may be variability in the definitions for different phases of labor, and what constitutes "normal" labor across studies and likely in practice as well. In order to better understand the impact of this variability on the evidence on specific interventions, we also review the evidence on the definition of "normal" labor progression.

The specific key questions (KQs) addressed in this review are listed below, and Figure A displays the analytic framework that guided our work.

- KQ 1: Do delivery outcomes for management of abnormal labor differ based on the criteria used to define protracted or arrested labor at different stages of the labor process?
- KQ 2: What are the benefits and harms of amniotomy in women in spontaneous labor?
- KQ 3: What are the benefits and harms of supportive care measures, including ambulation, nutrition, hydration, and emotional support during spontaneous labor?
- KQ 4: What are the benefits and harms of epidural analgesia in labor, particularly in terms of the risk of a diagnosis of prolonged labor?

- KQ 5: How does the frequency of cervical examination affect the probability of specific benefits and harms?
- KQ 6: What are the benefits and harms of intrauterine pressure catheters in the diagnosis and management of labor dystocia?
- KQ 7: For women with abnormal labor, what are the relative benefits and harms of high- versus low-dose oxytocin protocols (including nipple stimulation)?
- KQ 8: For women in spontaneous labor undergoing augmentation with oxytocin, what are the relative benefits and harms (in terms of both maternal and neonatal outcomes) of electronic fetal monitoring versus intermittent auscultation?
- KQ 9: For women in the second stage of labor, is there a benefit from delayed or Valsalva pushing for time to delivery or mode of delivery?

Figure A. Analytic framework



Abbreviations: AEs=adverse effects; KQ=Key Question; NICU=neonatal intensive care unit

Methods

Detailed methods are available in the full report and the posted protocol (http://effectivehealthcare.ahrq.gov/index.cfm).

Literature Search Strategy

To identify relevant published literature, we searched PubMed®, Embase®, CINAHL®, and the Cochrane Database of Systematic Reviews (CDSR), limiting the searches to studies published in English from January 1, 2005, to various dates in January 2016 (PubMed and Embase, January 12; CINAHL, January 20; CDSR, January 20). These databases were selected based on internal expert opinion that they would identify most of the relevant literature on this topic and that they reflect the databases used in related SRs, particularly reviews conducted by the Cochrane Pregnancy and Childbirth Group. An experienced search librarian guided all searches. The exact search strings used are given in Appendix A.

We supplemented the electronic searches with a manual search of citations from a set of key primary and review articles. The reference lists for identified key articles were manually searched and cross-referenced against our database, and additional relevant articles not already under consideration were retrieved for screening. All citations were imported into an electronic bibliographical database (EndNote® Version X7; Thomson Reuters, Philadelphia, PA).

To identify relevant gray literature, the EPC Scientific Resource Center notified stakeholders that the EPC was interested in receiving information relevant to the KQs. We also searched ClinicalTrials.gov for two purposes: (1) to identify relevant articles from completed studies that may not have appeared through other search strategies and (2) as one mechanism to ascertain publication bias in recent studies. For the latter goal, we sought to identify completed but unpublished studies that could impact the findings of the review. We also explored the possibility of publication bias specifically in our quantitative synthesis of the included literature through meta-analysis techniques such as funnel plots when appropriate. Further gray literature assessment included searching the World Health Organization International Clinical Trials Registry Platform search portal and the National Guidelines Clearinghouse to identify potentially relevant study records; we subsequently searched for relevant articles from among the completed studies.

We specified our inclusion and exclusion criteria based on the PICOTS (populations, interventions, comparators, outcomes, timing, and settings) identified for each question. For citations retrieved from PubMed, Embase, and the Cochrane Database of Systematic Reviews, two reviewers independently screened each title and abstract for potential relevance to the research questions using prespecified inclusion/exclusion criteria. Articles included by either reviewer underwent full-text screening. Articles meeting eligibility criteria at the full-text stage were included for data abstraction. Based on their clinical and methodological expertise, a pair of researchers were assigned to abstract data from each of the eligible articles. One researcher abstracted the data, and the second over-read the article and the accompanying abstraction to check for accuracy and completeness. Disagreements were resolved by consensus or by obtaining a third reviewer's opinion if consensus could not be reached.

Risk of Bias Assessment of Individual Studies

We assessed methodological quality, or risk of bias, for randomized and nonrandomized individual study designs using a components approach, assessing each study for specific aspects of design or conduct (such as allocation concealment for RCTs, or use of methods to address potential confounding), as detailed in AHRQ's *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[9] Briefly, we rated each study as being of good, fair, or poor quality based on its adherence to well-accepted standard methodologies. For each study, one investigator assigned a summary quality rating, which was then reviewed by a second investigator; disagreements were resolved by consensus or by a third investigator if agreement could not be reached.

Data Synthesis

We began by summarizing key features of the included studies for each KQ. To the degree that data were available, we abstracted information on study design; patient characteristics; clinical settings; interventions; and intermediate, final, and adverse event outcomes.

We then determined the feasibility of completing a quantitative synthesis (i.e., meta-analysis, decision analysis, or simulation model). For a meta-analysis, feasibility depends on the volume of relevant literature (requiring at least three relevant studies), conceptual homogeneity of the studies (similar intervention comparisons and outcome definitions), completeness of the reporting of results, and the adequacy and completeness of any existing meta-analyses (MAs).

Strength of the Body of Evidence

We graded the strength of evidence for each outcome assessed using the approach described in AHRQ's *Methods Guide*.[9-11] We also discussed the consistency of our findings with recent SRs, along with possible causes for disagreement and impact on strength of evidence ratings, in the results. Newly identified studies are presented separately from the results of existing reviews. Overall strength of evidence findings are based on the primary evidence, not the quality or number of existing SRs. A summary rating of high, moderate, or low strength of evidence was assigned for each outcome after discussion by two reviewers. When no evidence was available, or when evidence on the outcome was too weak, sparse, or inconsistent to permit any conclusion to be drawn, a grade of "insufficient" was assigned.

Results

We briefly summarize the results of our literature searches, description of included studies, key points, and strength of evidence for each KQ.

Summary of Studies

The literature search yielded 7,635 unique citations. In total, 787 full-text articles were retrieved and screened. Of these, 676 were excluded at the full-text screening stage, leaving 111 articles for data abstraction. These 111 articles described 105 unique studies. The relationship of studies to the review questions is as follows: 12 studies relevant to KQ 1, 8 studies relevant to KQ 2, 50 studies relevant to KQ 3, 22 studies relevant to KQ 4, 1 study relevant to KQ 5, 1 study relevant to KQ 6, 12 studies relevant to KQ 7, 0 studies relevant to KQ 8, and 2 studies relevant to KQ 9 (some studies were relevant to more than one KQ).

Key Question 1. Criteria Used to Define Abnormal Labor

We identified nine individual studies that examined whether labor outcomes among women in spontaneous labor differed based on the criteria used to define abnormal labor.[12-20] Key findings include:

- The use of a two-hour action line partogram compared with a four-hour action line partogram resulted in shorter total duration of labor (low strength of evidence [SOE]). Evidence was insufficient regarding rates of cesarean delivery.
- No differences were seen in postpartum hemorrhage rates (moderate SOE), neonatal acidemia rates (low SOE), or vaginal delivery rates (moderate SOE) between women managed with varying partogram strategies.
- Maternal satisfaction was also no different between partogram strategies (low SOE).
- Modern labor curves constructed from the Consortium on Safe Labor (CSL) demonstrate significantly different rates of cervical change, duration of labor, and appearance of the curve (absence or presence of an inflection point) between nulliparous and parous women.
- Modern labor curves constructed from the CSL cohort vary significantly from curves constructed from historical cohorts (Friedman or National Collaborative Perinatal Project [NCPP]), with modern curves suggesting a longer duration of the first stage of labor.
- Maternal age influences the duration of the first and second stage of labor among nulliparous women.

Table A summarizes the SOE for the use of partograms. In general, the SOE was reduced for outcomes because the evidence was based on findings from non-U.S. settings (and several studies focused on low-resource settings).

Table A. Partogram use: Strength of evidence for major outcomes and adverse events

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	1 RCT[19] (2,975)	**Improvement with 2-hour action line partogram:** An RCT in the UK demonstrated a shorter total duration of labor in women managed with a 2-hour action line partogram compared to women managed with a 4-hour action line partogram.	Low (Indirect [non-U.S. setting], 1 study)
Process Related Outcomes – Operative Vaginal Delivery	1 RCT[19] (1,929) 1 SR/MA[21] (7,706)	**No difference:** No difference in operative vaginal delivery rates between women managed with varying partogram strategies.	Moderate (non-U.S. setting)
Process Related Outcomes – Parental Preferences	1 RCT[19] (1,929)	**No difference:** An RCT in the UK demonstrated no difference in maternal satisfaction scores between women managed with a two-hour action line partogram compared to women managed with a four-hour action line partogram.	Low (non-U.S. setting, 1 study)
Adverse Events			
Maternal Outcomes – Hemorrhage	2 RCTs[19,20] (3,601)	**No difference:** No difference postpartum hemorrhage rates among women managed with varying partogram strategies.	Moderate (non-U.S. setting)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Neonatal Outcomes – Acidemia	1 RCT[19] (1,929)	**No difference:** No difference in neonatal acidemia rates between women managed with varying partogram strategies.	Low (non-U.S. setting, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SR/MA=systematic review/meta-analysis

Key Question 2. Amniotomy

We identified six RCTs that examined the benefits and harms of amniotomy (± oxytocin) in women in spontaneous labor.[22-27] Key findings include:

- Amniotomy decreases the total duration of labor in nulliparous women (moderate SOE).
- There were no differences in rates of maternal infection, hemorrhage, or trauma to the pelvic floor (moderate SOE) for early amniotomy versus control.
- Routine amniotomy plus oxytocin decreases the duration of labor and has a similar effect in both nulliparous and multiparous women (high SOE).
- Routine amniotomy plus oxytocin does not differ compared to control treatment in cesarean delivery rates in both nulliparous and multiparous women (high SOE).

Tables B–F summarize the SOE for amniotomy (± oxytocin) versus control treatment.

Table B. Early amniotomy versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	4 RCTs[22-24,27] (1473)	**Improvement with early amniotomy:** All four trials (2 fair quality, 2 good quality) demonstrated a decrease in the duration of labor in women randomized to early amniotomy.	Moderate (Medium risk of bias, Indirect)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table C. Early amniotomy versus control: Strength of evidence in women with unspecified parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[23,25] (411)	**No difference**: According to two good quality RCTs, there was no difference in the rate of cesarean delivery between women randomized to early amniotomy versus control.	Low (Indirect, imprecise)
Adverse Events			
Maternal Outcomes – Infection	2 RCTs[23,24] (973)	**No difference:** There was no evidence of increased risk of infection associated with early amniotomy versus control.	Moderate (Imprecise)
Maternal Outcomes – Hemorrhage	2 RCTs[23,24] (973)	**No difference:** There was no evidence of increased risk of maternal hemorrhage associated with early amniotomy.	Moderate (Imprecise)
Maternal Outcomes – Trauma to Pelvic Floor	3 RCTs[23,24,27] (683)	**No difference:** There was no evidence of increased risk of trauma to the pelvic floor associated with early amniotomy.	Moderate (Medium risk of bias)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Neonatal Outcomes – Infection	1 RCT[24] (690)	**No difference:** There was no evidence of increased risk of neonatal infection associated with early amniotomy.	Low (1 study)
Process Related Outcomes – Mode of Delivery (Operative Vaginal Delivery)	3 RCTs[23,25,27] (611)	**No difference:** There was no evidence of increased risk of operative vaginal delivery associated with early amniotomy.	Low (Indirect, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table D. Amniotomy plus oxytocin versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[23,26] (1,243) 3 SR/MAs[28-30] (11,167)	**Improvement with amniotomy plus oxytocin:** Amniotomy plus oxytocin decreased the duration of the first stage of labor.	High
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[23,26] (1,243) 2 SR/MAs[28,29] (8,496)	**No difference:** There was no difference in the duration of second stage of labor between groups.	Moderate (Imprecise)
Process Related Outcomes – Duration of Total Labor	2 RCTs[23,26] (1,243) 3 SR/MAs[28-30] (13,312)	**Improvement with amniotomy plus oxytocin:** The duration of labor was shortened in women randomized to amniotomy plus oxytocin as compared to routine care.	High
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[23,26] (1,243) 3 SR/MAs[28-30] (16,529)	**No difference:** Based on SR and included RCTs, there was no difference in cesarean delivery rates between amniotomy plus oxytocin compared with control	High

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR/MA=systematic review/meta-analysis

Table E. Amniotomy plus oxytocin versus control: Strength of evidence in women with unspecified parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[23] (283) 3 SR/MAs[28-30] (11,167)	**Improvement with amniotomy plus oxytocin:** Based on SR/MAs and included RCTs, amniotomy plus oxytocin decreased the duration of the first stage of labor.	High
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[23] (283) 2 SR/MAs[28,29] (8,496)	**No difference:** There was no difference in the duration of the second stage of labor in the amniotomy plus oxytocin group as compared with control.	Moderate (Imprecise)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Duration of Total Labor	1 RCT[23] (283) 3 SR/MAs[28-30] (13,312)	**Improvement with amniotomy plus oxytocin:** Based on SR/MAs and included RCTs, amniotomy plus oxytocin decreased the total duration of labor.	High
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[23] (283) 3 SR/MAs[28-30] (16,529)	**No difference:** Based on SR/MAs and included RCTs, there was no difference in cesarean delivery rates between amniotomy plus oxytocin compared with control.	High
Adverse Events			
Maternal Outcomes – Infection	3 RCTs[23,24,26] (1,933) 3 SR/MAs[28-30] (11,419)	**No difference:** There was no difference in risk of infection between groups.	High
Maternal Outcomes – Hemorrhage	1 RCT[23] (283) 3 SR/MAs[28-30] (11,311)	**No difference:** No difference in risk of hemorrhage between groups.	High
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[23] (283)	**No difference:** One RCT examined active management of labor with early amniotomy and oxytocin as compared with routine care, there was no difference in risk of trauma to the pelvic floor between groups.	Low (1 study)
Process Related Outcomes – Mode of Delivery (Operative Vaginal Delivery	2 RCTs[23,26] (1,243) 2 SR/MAs[29,30] (3,096)	**No difference:** There was no difference in risk of operative vaginal delivery between groups.	High
Process Related Outcomes – Parental Preferences	1 RCT[23] (283) 3 SR/MAs[28-30] (11,114)	**No difference:** No difference between the two groups in scores of maternal/parental satisfaction.	Moderate (Imprecise, varying metrics)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR/MA=systematic review/meta-analysis

Table F. Amniotomy plus oxytocin versus control: Strength of evidence in multiparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[23] (283) 3 SR/MAs[28-30] (11,167)	**Improvement with amniotomy:** Amniotomy decreased the duration of the first stage of labor compared with control	Moderate (Imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[23] (283) 2 SR/MAs[28,29] (8,496)	**No difference:** No difference in the duration of second stage of labor between groups.	Moderate (Imprecise)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Duration of Total Labor	1 RCT [23] (283) 3 SR/MAs[28-30] (13,312)	**Improvement with amniotomy plus oxytocin:** Modest decrease in duration of labor in the intervention group as compared with controls.	Moderate (Imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[23] (283) 3 SR/MAs[28-30] (16,529)	**No difference:** No difference in the rate of cesarean delivery between groups.	Moderate (Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR/MA=systematic review/meta-analysis

Key Question 3. Supportive Care

We identified 44 articles[31-74] representing 42 individual RCTs that examined the benefits and harms of supportive care measures in women during spontaneous labor. Key findings include:

- Supportive care measures during labor encompass a wide variety of interventions and within individual categories of interventions, there is considerable heterogeneity in the nature and timing of the interventions.
- Although supportive care therapies are often seen as benefiting parental satisfaction with the birthing process, these outcomes were only assessed in 5 of our included RCTs with sparse evidence. An existing SR of 11 studies however did find that women receiving continuous emotional support were less likely to rate their birth experience negatively (moderate SOE).
- Two studies addressing continuous emotional support included in the present review did not show a benefit in reducing 1st or 2nd stage labor duration, although prior SR/MAs of 12 studies (including these two studies) indicated a benefit for total labor duration (moderate SOE).
- Emotional support interventions reduced cesarean deliveries (low SOE for doula support, moderate SOE for continuous emotional support) and instrumental deliveries (moderate SOE).
- There was no difference in rates of cesarean deliveries for women receiving perineal compresses or massage (low SOE), but severe perineal trauma was reduced in nulliparous women (low SOE).
- There was no difference in duration of labor in women using water birth (low SOE)
- Women undergoing acupuncture/acupoint nerve stimulator did not experience differences in labor duration or rates of maternal hemorrhage (low SOE for both outcomes).
- Ambulation was associated with reduced duration of duration of labor (low SOE).
- No differences were found in duration of labor (low SOE) or cesarean delivery rates (moderate SOE) for women using differing positioning interventions. Women in kneeling position were more likely than women in sitting position to have reduced trauma to the pelvic floor (low SOE).
- Administration of intravenous fluids compared with oral intake alone demonstrated a reduction in the duration of labor (low SOE), while not increasing cesarean delivery rates (moderate SOE), maternal hemorrhage (low SOE), or operative vaginal delivery rates (moderate SOE).

Table G summarizes the SOE for continuous emotional support versus control in nulliparous women. Strength of evidence for continuous emotional support versus control in women of mixed parity was rated as insufficient for all outcomes.

Table G. Continuous emotional support versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[63,74] (326)	**No difference:** Good-quality studies of nulliparous women found that continuous emotional support did not reduce duration of 1st stage labor.	Moderate (Indirect)
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[63,74] (326)	**No difference:** Good-quality studies of nulliparous women found that continuous emotional support did not reduce duration of 2nd stage labor.	Moderate (Indirect)
Process Related Outcomes – Duration of Total Labor	1 SR[75] (5,366)	**Improvement with continuous emotional support:** Systematic review of 12 studies found shorter total duration of labor (mean difference -0.58 hr, 95% CI -0.85 to -0.31).	Moderate (Indirect)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[54,63] (599) 2 SRs[75,76] (17,583)	**Improvement with Doula support:** Doula support reduced cesarean deliveries as compared to control therapy. Existing SR of 5 studies demonstrated reduced risk of cesarean delivery with doula support. The inconsistency amongst our 2 included RCTs lowered the SOE to low. **Improvement with continuous emotional support:** Continuous emotional support lowered risk of cesarean delivery (RR 0.78, 95% CI 0.67 to 0.91) based on SR of 22 studies.	Low – Doula (Indirect, inconsistent) Moderate – Continuous Emotional Support (Indirect)
Process Related Outcomes – Mode of Delivery (Instrumental Delivery)	2 SRs[75,76] (15,705)	**Improvement with Doula support:** Doula support reduced risk of instrumental vaginal delivery (OR 0.54, 95% CI 0.35 to 0.92). **Improvement with continuous emotional support:** Continuous emotional support lowered risk of instrumental vaginal delivery (RR 0.90, 95% CI 0.85 to 0.96) based on SR of 19 studies.	Moderate (Indirect)
Adverse Events			
Process Related Outcomes – Abnormal Fetal Heat Tracing	1 RCT[63] (212)	**No difference:** Supportive care was not associated with significant differences in fetal heart tracings.	Low (Indirect, imprecise, 1 study)
Process Related Outcomes – Parental Preferences	1 SR[75] (11,113)	**Improvement with continuous emotional support:** SR of 11 studies found women receiving continuous emotional support less likely to rate their birth experience negatively (RR 0.69, 95% CI 0.59 to 0.79).	Moderate

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: CI=confidence interval; hr=hours; RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence; SR=systematic review

Tables H–K summarize the SOE for perineal compresses or massage versus control in nulliparous women and women of mixed parity. In general the SOE was rated as low given evidence from only one study.

Table H. Perineal compresses or massage versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[71] (717)	**No difference:** No significant differences in the proportion of cesarean deliveries was reported for the massage/compress group.	Low (Indirect, 1 study)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[71] (717)	**Improvement with massage/compress:** Severe perineal trauma (third- and fourth-degree perineal laceration) was lower incidence for the massage/compress group (OR 2.16, 95% CI 1.15 to 4.10).	Low (1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; OR=odds ratio; RCT=randomized controlled trial; SOE=strength of evidence

Table I. Perineal compresses or massage versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[60] (1,211)	**No difference:** Duration of 2nd stage labor was not statistically significantly different between the intervention and usual care groups.	Low (Indirect, 1 study)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[60] (1,211)	**No difference:** No significant differences in the proportion of cesarean deliveries was reported for the massage/compress group.	Low (Indirect, 1 study)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[60] (1,211)	**No difference:** No significant differences in perineal trauma were reported between the intervention and control groups.	Low (1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table J. Massage during labor versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	2 RCTs[40,41] (123)	**No difference:** Total duration of labor was not significantly different in the massage group compared to usual care.	Low (Indirect, Imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[40,41] (123)	**No difference:** The proportion of cesarean deliveries was not significantly different between the massage group and control group.	Low (Indirect, Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table K. Water birth versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[52] (106) 1 SR[77] (286)	**No difference:** No difference in duration of 2nd stage labor was reported between the water birth and usual care groups. SOE was increased to low given findings from SR which also demonstrated no difference between water birth versus control.	Low (Medium risk of bias, indirect, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

For the studies which compared acupressure versus control, although findings were consistent between studies, the SOE was rated as insufficient for all outcomes given the small number of patients, the potential risk of bias, and the imprecision of the findings.

Tables L and M summarize the SOE for acupuncture/acupoint nerve stimulator versus control therapy. Other than the outcomes listed below, the SOE was rated as insufficient for all other outcomes given inconsistent findings from studies with variability in interventions.

Table L. Acupuncture/acupoint nerve stimulator versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[31,50] (350)	**No difference:** No significant difference in 2nd stage labor between the acupuncture and control groups was reported.	Low (Medium risk of bias, indirect, Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table M. Acupuncture/acupoint nerve stimulator versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[31,50] (350)	**No difference:** No significant difference in 2nd stage labor between the acupuncture and control groups was reported.	Low (Medium risk of bias, indirect, imprecise)
Adverse Events			
Maternal Outcomes – Hemorrhage	1 RCT[37] (253)	**No difference:** No significant difference in hemorrhage was reported for the intervention group compared to the control.	Low (High risk of bias, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

The SOE findings for all outcomes comparing aromatherapy and control treatment was rated as insufficient given the potential risk of bias, small study size, and inconsistent findings. The SOE findings for outcomes comparing *Anetheum graveolens* seeds (dill) and control treatment was rated as insufficient.

Tables N–P summarize the SOE for ambulation or positioning versus control therapy. Overall the SOE was reduced given the potential risk of bias in the included studies.

Table N. Ambulation versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[61,64] (271)	**Improvement with ambulation:** 1 good-quality[64] and 1 poor-quality study[61] found that ambulation was associated with significantly reduced duration of the first stage and total duration of labor. SOE was reduced given the quality of the studies and imprecision of the findings.	Low (Medium risk of bias, indirect, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Table O. Positioning versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	4 RCTs[49,55,58,70] (608)	**No difference:** None of four studies examining use of a birth ball, kneeling, sitting, or semi-sitting laboring positions found statistically significant differences in duration of active labor. The SOE was reduced given the potential risk of bias and variation in interventions.	Low (High risk of bias, indirect, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[43,58] (1,273) 1 SR[78] (2079)	**No difference:** No significant differences were found between the intervention and control groups in mode of delivery. The SOE was increased given the support of a meta-analysis of 11 studies.	Moderate (Medium risk of bias, indirect, imprecise)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[58] (271)	**Improvement with kneeling:** Women in kneeling position were more likely than women in sitting position to have an intact peritoneum (51 vs. 37%) and fewer 3rd or 4th degree tears (3 vs. 6%).	Low (Imprecise, one study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Table P. Positioning versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCT[56,65] (401)	**Improvement with positioning:** Second stage of labor was significantly shorter in women using either a peanut ball or a squatting position.	Low (Medium risk of bias, indirect, Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table Q summarizes the SOE for nutritional, oral, or parenteral hydration interventions in nulliparous women. The SOE was insufficient for outcomes in women of mixed parity.

Table Q. Specific nutritional or oral or parenteral hydration recommendations or limitations: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	3 RCTs[39,44,57] (861) 1 SR[79] (1,781)	**Improvement with intravenous fluids:** Administration of intravenous fluids compared with oral intake alone demonstrated a reduction in the duration of labor. The SOE was reduced given the inconsistency in the findings of individual trials and the variability in hydration strategies.	Low (Indirect, inconsistent, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	6 RCTs[39,45,48,51,53,57] (1,373)	**No difference:** No significant differences were found between groups of women receiving oral hydration versus high-level intravenous hydration (OR 1.26, 95% CI 0.08 to 18.84)	Moderate (Indirect, Imprecise)
Adverse Events			
Maternal Outcomes – Hemorrhage or Infection	2 RCTs[44,53] (539)	**No difference:** No significant differences in rates of maternal hemorrhage or infection were found between groups of women receiving infusions of 5% or 10% dextrose and normal saline.	Low (Imprecise)
Process Related Outcomes – Mode of Delivery (Operative Vaginal Delivery)	5 RCTs[39,44,51,57] (1,234)	**No difference:** No difference in operative vaginal delivery rates amongst 5 studies using varying methods of hydration.	Moderate (Indirect, Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; OR=odds ratio; RCT=randomized controlled trial; SOE=strength of evidence

Key Question 4. Epidural Analgesia

We identified 22 articles[31,80-100] representing 19 individual RCTs that examined the benefits and harms of epidural analgesia (EA) in labor. Key findings included:

- For nulliparous women, a meta-analysis showed no significant differences between EA and combined spinal epidural (CSE) in duration of the first stage of labor (low SOE) or duration of the second stage of labor (low SOE). However, total duration of labor (from time of intervention to delivery) was significantly longer for EA relative to CSE (moderate SOE). There were no differences between EA and CSE in rates of cesarean delivery (moderate SOE).
- For women of mixed parity, there was no difference between EA and CSE for total duration of labor (low SOE), or rates of cesarean delivery (moderate SOE).
- For women of mixed parity, there were no differences between EA and patient-controlled intravenous analgesia (PCIA) in duration of labor or rates of cesarean delivery (low SOE for both outcomes).
- For nulliparous women, there was no difference in duration of first or second stage labor or rates of cesarean delivery for early versus late EA (moderate SOE for all outcomes

- For women of mixed parity, there was no evidence of a difference between EA and no EA for the duration of the first stage of labor or rates of cesarean delivery. There was a slight increase in the duration of the second stage for women with EA (moderate SOE for all outcomes).

Tables R and S summarize the SOE for epidural analgesia (EA) versus combined spinal epidural analgesia (CSE). In general, meta-analysis of the included studies allowed low and moderate SOE for major outcomes of interest.

Table R. Epidural analgesia versus combined spinal epidural: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	5 RCTs[83,87,89,95,100] (1,424)	**No difference:** Meta-analysis showed no significant differences between EA and CSE in duration of the first stage of labor (mean difference [MD] 32.7 minutes; 95% CI -19.3 to 84.7).	Low (Medium risk of bias, indirect, inconsistent, imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	5 RCTs[83,87,89,95,100] (1,424)	**No difference:** Meta-analysis showed no significant differences between EA and CSE in duration of the second stage of labor (MD -0.2 minutes; 95% CI -21.9 to 21.6).	Low (Medium risk of bias, indirect, inconsistent, imprecise)
Process Related Outcomes – Total Duration of Labor	5 RCTs[83,87,89,95,100] (1,424)	**Worsening with EA:** Meta-analysis showed total duration of labor (from time of intervention to delivery) was significantly longer for EA relative to CSE, with an MD of 62.0 minutes (95% CI 7.2 to 116.7).	Moderate (Medium risk of bias, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	5 RCTs[83,87,93,95,100] (1,604)	**No difference:** Meta-analysis of the data from 1604 patients in these 5 RCTs showed no statistically significant difference in cesarean delivery rates between EA and CSE (odds ratio [OR] 1.1; 95% CI 0.9 to 1.2).	Moderate (Indirect)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; MD=mean difference; OR=odds ratio; RCT=randomized controlled trial; SOE=strength of evidence

Table S. Epidural analgesia versus combined spinal epidural: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Total Duration of Labor	2 RCTs[82,89] (258)	**No difference:** No significant difference between EA and CSE for total duration of labor.	Low (Medium risk of bias, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	4 RCTs[82,89,92,94] (374)	**No difference:** Meta-analysis generated an estimate of the odds ratio of cesarean delivery associated with CSE relative to EA of 0.8 (95% CI: 0.5 to 1.3).	Moderate (Medium risk of bias)
Adverse Events			
Process Related Outcomes – Abnormal Fetal Heart Tracing	2 RCTs[82,94] (190)	**Improvement with EA:** CSE was associated with a higher proportion of patients with abnormal fetal heart rate tracings than EA in one study and a risk ratio of 2.28 (95% CI: 0.64 to 8.16) for an abnormal fetal heart tracing in another study.	Low (Medium risk of bias, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; RCT=randomized controlled trial; SOE=strength of evidence

Table T summarizes the SOE for EA versus patient-controlled intravenous analgesia. In general, the SOE was judged insufficient for outcomes given the imprecision of the findings, findings for specific outcomes from just one study, and the non-U.S. settings. Low SOE was reported for duration of labor and cesarean delivery in women with mixed or unspecified parity.

Table T. Epidural analgesia versus patient-controlled intravenous analgesia: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Total Duration of Labor	3 RCTs[31,86,91] (177)	**No difference:** Meta-analysis did not identify differences in duration of labor, with the estimated mean after EA administration minus duration after PCIA being -10.1 minutes (95% CI -134.3 to 114.1).	Low (Medium risk of bias, imprecise, non-U.S. settings)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	3 RCTs[31,86,91] (17)	**No difference:** Meta-analysis generated an estimate of the odds ratio for cesarean delivery of EA relative to PCIA of 1.3 (95% CI 0.3 to 5.6).	Low (Medium risk of bias, imprecise, non-U.S. settings)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; EA=epidural analgesia; PCIA=patient-controlled intravenous analgesia; RCT=randomized controlled trial; SOE=strength of evidence

The SOE findings for EA versus intravascular tramadol in women of mixed parity was rated as insufficient for all outcomes. Table U summarizes the SOE for early versus late epidural analgesia. The SOE was rated as moderate for all outcomes based on evidence from the SR. The SOE was lowered given that the included studies from the SR spanned 1994 to 2006.

Table U. Early versus late epidural analgesia: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 SR[101] (6 studies, 1,739 patients)	**No difference:** No differences between early and late EA with an odds ratio of 0.95 (95% CI 0.81 to 1.10).	Moderate
Process Related Outcomes – Duration of 2nd Stage Labor	1 SR[101] (6 studies, 1,690 patients)	**No difference:** No differences between early and late EA with a weighted mean difference of 0.52 minutes (95% CI -5.03 to 6.06 minutes)	Moderate
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 SR[101] (8 studies, 2,980 patients)	**No difference:** No differences between early and late EA (odds ratio=1.00, 95% CI 0.83 to 1.21)	Moderate

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Strength of evidence was rated as insufficient for all outcomes of these comparisons:

- Routine EA versus analgesia on request
- CSE versus nonpharmacologic pain relief
- EA versus intravenous meperidine

- EA versus low-dose infusion EA
- EA acupuncture point nerve stimulation
- EA versus no EA in nulliparous women

Table V summarizes the SOE for outcomes comparing EA versus no EA in women of mixed parity. The SOE was rated as moderate for major outcomes of labor duration and cesarean delivery based on the findings from a large SR.

Table V. Epidural analgesia versus no epidural analgesia: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – 1st Stage of Labor	1 RCT[31] (120) 1 SR[102] (11 studies 2981 patients)	**No difference:** No evidence of a significant difference between EA and no EA (MD 18.51 minutes, 95% CI -12.91 to 49.42)	Moderate
Process Related Outcomes – 2nd Stage of Labor	1 RCT[31] (120) 1 SR[102] (13 studies 4233 patients)	**Worsening with EA:** Women with epidural analgesia had a statistically significant longer second stage of labor (average MD 13.66 minutes, 95% CI 6.67 to 20.66).	Moderate
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[31] (120) 1 SR[102] (27 studies 8417 patients)	**No difference:** No evidence of a significant difference in the risk of caesarean section overall (RR 1.10, 95% CI 0.97 to 1.25).	Moderate

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; EA=epidural analgesia; MD=mean difference: RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence; SR=systematic review

Key Question 5. Frequency of Cervical Examination

We identified no RCTs and only one good-quality SR[103] that met the inclusion criteria for this KQ. The focus of the SR was to compare different methods of assessing labor progression through the use of vaginal examinations. The objective was to compare digital vaginal examinations for assessing progress of labor to other strategies or different timings. There was insufficient SOE for all outcomes regarding the frequency of cervical examination.

Key Question 6. Intrauterine Pressure Catheters

We did not identify any RCTs that met the inclusion criteria for this KQ. One good-quality SR addressed the benefits and harms of intrauterine pressure catheters in the diagnosis and management of labor dystocia.[104] There were no statistically significant differences between intrauterine pressure catheters and external uterine monitoring for the outcomes of mode of delivery, mean time to delivery, neonatal acidemia, or admission to the NICU (moderate SOE for all outcomes).

Table W summarizes the SOE for intrauterine pressure catheters versus external monitoring. The SOE was rated as moderate for all outcomes assessed given consistent findings from good-quality RCTs included in the SR.

Table W. Intrauterine pressure catheters versus external monitoring: Strength of evidence in women of unspecified parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	1 SR/MA[104] of 1 RCT (1456)	**No difference:** No differences in mean time to delivery with intrauterine pressure catheters compared to external monitoring	Moderate (Indirect)
Process Related Outcomes – Mode of Delivery	1 SR/MA[104] of 2 RCTs (750)	**No difference:** Comparing intrauterine pressure catheters to external monitoring, there was no difference in delivery by operative vaginal delivery (RR 1.25, 95% CI 0.91 to 1.73) or by cesarean deliver (RR 1.25, 95% CI 0.91 to 1.71).	Moderate (Indirect)
Adverse Events			
Maternal Outcomes – Infection	1 SR/MA[104] of 1 RCT (1456)	**No difference:** No differences in signs of infection in labor in women with intrauterine pressure catheters compared to external monitoring (RR 0.69, 95% CI 0.44 to 1.08).	Moderate (Indirect)
Neonatal Outcomes – Acidemia	1 SR/MA[104] of 1 RCT (1456)	**No difference:** No differences in neonatal acidemia (pH<7.15) in infants of women with intrauterine pressure catheters compared to external monitoring (RR 1.31, 95% CI 0.95 to 1.79).	Moderate (Indirect)
Neonatal Outcomes – Admission to NICU	1 SR/MA[104] of 2 RCTs (489)	**No difference:** No differences in admission to NICU in infants of women with intrauterine pressure catheters compared to external monitoring (RR 0.34, 95% CI 0.07 to 1.67).	Moderate (Indirect)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: CI=confidence interval; NICU=neonatal intensive care unit; RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence; SR/MA=systematic review/meta-analysis

Key Question 7. High-Dose versus Low-Dose Oxytocin Protocols

We identified eight articles[23,26,105-110] representing seven individual RCTs that examined the benefits and harms of high-dose versus low-dose oxytocin protocols for women with abnormal labor. Key findings include:

- High-dose oxytocin is associated with a lower cesarean delivery rate compared with low-dose oxytocin protocols (moderate SOE).
- Early administration of oxytocin is associated with a shorter duration of labor (high SOE) but does not affect the overall cesarean delivery rate compared with delayed administration (high SOE). There are no difference in adverse events.
- Pulsatile administration of oxytocin is associated with a longer duration of labor compared with continuous administration (low SOE).
- There is no difference in cesarean delivery rate between women managed with oxytocin compared to expectant management (low SOE).

Tables X–AA summarize the SOE for varying oxytocin protocols strategies. For many outcomes the SOE was rated as insufficient or low except where existing SRs were able to add to the evidence base.

Table X. High-dose versus low-dose oxytocin protocols: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[26,105] (1,052) 2 SRs[111,112] (9 studies, 945 patients)	**Improvement with high-dose oxytocin:** High- dose oxytocin augmentation was associated with a reduction in the risk of cesarean section supported by 2 RCTs and 2 SRs. There was however inconsistency in findings and substantial heterogeneity reducing the SOE.	Moderate (imprecise)
Adverse Events			
Maternal Outcomes – Infection	2 RCTs[26,105] (1,052)	**No difference:** A small, pilot RCT demonstrated no difference in the rate of maternal infection by oxytocin dosing protocol. A good-quality RCT in Thailand showed no difference in the rate of maternal infection between high-and low-dose oxytocin as part of an active management of labor protocol compared to a conventional management of labor protocol.	Low (Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Table Y. Early versus delayed oxytocin protocols: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Labor	2 SR[113,114] (10 studies, 2583 patients)	**Improvement with early oxytocin:** Reduction in the overall duration of labor between women managed with early versus delayed oxytocin administration.	High
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 SR[113,114] (10 studies, 2583 patients)	**No difference:** No differences in rates of cesarean delivery between women managed with early versus delayed oxytocin administration (RR 0.88, 95% CI 0.66 to 1.19)	High
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[107] (630)	**No difference:** An RCT of nulliparous women with prolonged labor from 2 delivery units in Sweden demonstrated no differences in perineal lacerations between women managed with early versus delayed oxytocin administration.	Low (Imprecise)
Maternal Outcomes – Transfusion	2 RCTs[107,109] (1,042)	**No difference:** 2 RCTs, 1 from the UK and 1 from Sweden both each demonstrated no differences in rates of maternal transfusion between women managed with early versus delayed oxytocin administration.	Moderate
Maternal Outcomes – Hemorrhage	2 RCTs[107,109] (1,042)	**No difference:** 2 RCTs, 1 from the UK and 1 from Sweden both each demonstrated no differences in rates of maternal postpartum hemorrhage between women managed with early versus delayed oxytocin administration.	Moderate

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Neonatal Outcomes – Neonatal Infection/Sepsis	1 RCT[109] (412)	**No difference:** An RCT of nulliparous women with dysfunctional labor from 12 delivery units in the UK demonstrated no differences in rates of neonatal infection/sepsis between women managed with early versus delayed oxytocin administration.	Low (1 study)
Neonatal Outcomes – Neonatal Acidemia	1 RCT[107] (630)	**No difference:** An RCT of nulliparous women with prolonged labor from two delivery units in Sweden demonstrated no differences in neonatal acidemia between women managed with early versus delayed oxytocin administration.	Low (1 study)
Process Related Outcomes – Mode of Delivery (Instrumental Delivery)	2 RCTs[107,109] (1,042)	**No difference:** 2 RCTs, 1 from the UK and 1 from Sweden both each demonstrated no differences in rates of operative vaginal delivery between women managed with early versus delayed oxytocin administration.	Moderate
Process Related Outcomes – Mode of Delivery (Spontaneous)	2 RCTs[107,109] (1,042)	**No difference:** 2 RCTs, one from the UK and one from Sweden both each demonstrated no differences in rates of spontaneous vaginal delivery between women managed with early versus delayed oxytocin administration.	Moderate

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence; SR=systematic review

Table Z. Pulsatile versus continuous oxytocin protocols: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[106] (487)	**No difference:** No difference in the duration of the second stage of labor among women managed with pulsatile compared to continuous oxytocin for augmentation of labor.	Low (Indirect, Imprecise)
Process Related Outcomes – Duration of Labor	1 RCT[106] (481)	**Improvement with continuous oxytocin:** Women managed with pulsatile compared to continuous oxytocin for augmentation of labor had a longer duration of labor.	Low (Indirect, imprecise)
Adverse Events			
Process Related Outcomes – Mode of Delivery (Operative delivery)	1 RCT[106] (500)	**No difference:** No difference in operative delivery rate between women managed with pulsatile compared to continuous oxytocin for augmentation of labor. The cesarean delivery rate was not reported.	Low (Indirect, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table AA. Oxytocin versus expectant management: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[23] (99) 1 SR[114] (3 studies, 138 patients)	**No difference:** No difference in cesarean delivery rate between women managed with oxytocin compared to expectant management.	Low (Imprecise)
Adverse Events			
Process Related Outcomes – Mode of Delivery (Instrumental Delivery)	1 RCT[23] (99) 1 SR[114] (3 studies, 138 patients)	**No difference:** No difference in operative vaginal delivery rate between women managed with oxytocin compared to expectant management.	Low (Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Key Question 8. Electronic Fetal Monitoring versus Intermittent Auscultation

We were unable to identify any relevant RCTs that met our inclusion criteria for this KQ. We identified 4 potential SRs that compared electronic fetal monitoring with intermittent auscultation,[115-118] but these were ultimately excluded because the studies included in the SRs utilized interventions that are not currently used in the United States.

Key Question 9. Timing of Pushing in the Second Stage

We identified three articles[119-121] representing two individual RCTs that examined pushing techniques. Key findings include:

- There is insufficient evidence on whether instruction on Valsalva pushing shortens the duration of the second stage of labor in nulliparous women when compared with instruction to push spontaneously or without coaching.
- Valsalva/coached and spontaneous/uncoached pushing have similar risks of trauma to the pelvic floor (low SOE).
- There was no evidence comparing the timing of pushing (immediate versus delayed) or Valsalva pushing versus spontaneous pushing in multiparous women.

Table BB summarizes the SOE for spontaneous pushing versus valsalva pushing. In general, SOE was judged insufficient for all outcomes, with the exception of the maternal outcome of trauma to the pelvic floor.

Table BB. Spontaneous pushing versus valsalva pushing: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	2 RCTs[119-121] (420)	**No difference:** Two RCTs reported no difference in the risk of trauma to the pelvic floor between Valsalva/coached and spontaneous/uncoached pushing strategies.	Low (Medium risk of bias, Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Discussion

In this comparative effectiveness review, we reviewed 105 studies described in 111 publications relevant to criteria used to define protracted or arrested labor (KQ 1); the benefits and harms of amniotomy (KQ 2), supportive care measures (KQ 3), and epidural analgesia (KQ 4) in spontaneous labor; the benefits and harms of cervical examination frequency (KQ 5) and intrauterine pressure catheters (KQ 6) in diagnosis and management of abnormal labor; the benefits and harms of high- and low-dose (including nipple stimulation) oxytocin augmentation in women diagnosed with abnormal labor progression (KQ 7); the benefits and harms of electronic fetal monitoring versus intermittent auscultation in women undergoing oxytocin augmentation (KQ 8); and the benefit of delayed or Valsalva pushing during the second stage of labor (KQ 9).

Findings in Relation to What is Already Known

In general, the findings of the review were consistent with current understanding of the overall strength of evidence for different strategies for management of labor. Estimates of the rate of progress of "normal" labor derived from contemporary data in the United States are quite different from the classic curves described by Friedman.[8] These differences may be attributable to a number of factors, including secular trends in patient characteristics (e.g., increasing age at first birth and increasing rates of obesity) and increasing use of interventions such as induction of labor or the use of oxytocin to augment labor. More recent data suggest that the transition to active labor occurs later in the course of labor than originally described, which is reflected in more recent guidelines suggesting a higher threshold for observing labor duration before intervention with cesarean delivery.

The definition of "normal" labor is fundamental in evaluating the evidence related to managing "abnormal" labor progression, analogous to the threshold value used to define "normal" for a continuous laboratory value. The sensitivity and specificity of the test will vary depending on the choice of threshold, but so will the estimates of the effectiveness of interventions based on that threshold. Comparing results across studies requires a common definition for such "normal" labor and permeates our review.

There is evidence that partograms are useful in low-resource settings, but they have not been shown to improve labor outcomes in high-resource settings. This may be due in part to differences in the data sources for generating labor curves and thresholds.

In general, our findings regarding other interventions are consistent with current guidelines [3], which are largely informed by the CSL data and encourage allowing longer durations for both first and second stages of labor before intervening with cesarean delivery. Routine amniotomy is not specifically recommended, although the recommendations note that amniotomy may be helpful in the transition from latent to active labor. Based on the same Cochrane review finding, improved satisfaction and lower cesarean and operative vaginal delivery rates, emotional support is recommended. The potential effect of epidural analgesia on duration of labor is noted as a potential consideration in allowing longer durations before intervention, but there are no recommendations about specific techniques. Cervical exam frequency, intrauterine pressure monitoring, oxytocin dosing protocols, methods for routine fetal monitoring, or timing of pushing in the second labor are not discussed, consistent with the relative paucity of evidence.

The impact of regional anesthesia on the length of the first stage of labor is uncertain, leading to conflicting recommendations from different professional societies. Our findings do not provide greater clarity.

Applicability

Two broad issues relate to the overall applicability of the available evidence to clinical practice in the United States—one geographic and one temporal. Many of the RCTs meeting our criteria were performed outside of the United States. Aside from issues related to differences in study oversight or reporting, the populations of these studies may differ from U.S. women in labor in terms of health systems, patient preferences and expectations, provider perceptions of risk, availability of resources, and so on. This is particularly relevant to studies that directly compared management strategies based on explicit criteria for defining abnormal labor and studies that attempted to define a "normal" duration of labor (KQ 1). Particularly for studies where the primary outcome is cesarean delivery, factors that affect the threshold for performing cesarean—both the explicit "cutpoint" for duration of labor used and broader factors ranging from the relative safety of surgery versus vaginal delivery in low resource settings to cultural expectations to legal concerns—may affect the estimates of effectiveness of an intervention.

A number of studies included the use of a partogram—a graphical comparison of a woman's labor progress compared to a standard—with thresholds for intervention clearly identified. Strength of evidence was judged to be low, with one major factor being a lack of U.S.-based studies. In low-resource settings, the use of a partogram was associated with lower overall cesarean delivery rates compared with labor managed without a partogram, and earlier interventions were associated with lower cesarean delivery rates. In high-resource settings, the use of a partogram that included an assessment of latent phase duration, and which had a threshold for action at 3 hours compared to 4 hours, had higher cesarean delivery rates; but otherwise the use of a partogram compared with no partogram, or other time intervals for action lines, did not affect mode of delivery, duration of labor, indication for cesarean delivery, or complications including postpartum hemorrhage, maternal infection, or neonatal acidemia. Outside of U.S.-based settings, populations, health systems, and management of both prenatal and intrapartum care are quite different—and the impact of these differences on both the relative effectiveness and the absolute difference in outcomes is likely substantial.

Even more fundamentally, use of a tool such as a partogram, or specific interventions such as amniotomy, requires evidence on "normal" labor in order to define appropriate thresholds for action. The studies we reviewed that attempted to define "normal" labor differed based on parity, the time period in which the studies were conducted, and, among nulliparous women, maternal age. Evidence from the Consortium on Safe Labor (CSL), representing the most recent available large-scale population data[14] suggest a longer duration of first stage of labor compared to earlier studies, including the National Collaborative Perinatal Project.[17] However, the most striking difference between these two studies was the proportion of women who received oxytocin augmentation (14.6% in the NCPP cohort from 1959 to 1966 compared with 45.9% in the CSL cohort from 2002 to 2008).

The CSL population that was used to generate new labor curves consists of women who had spontaneous onset of labor and a vaginal delivery, and thus the labor curves presented provide an estimate of "normal" labor that does not end in a cesarean delivery. Since such a large proportion of women received augmentation, these data do not provide insight into the range of rates of labor progression among women who do not receive augmentation, and cannot provide insight into the relative harms and benefits of augmentation, or the most appropriate thresholds for the timing or dosing of augmentation. The association between a longer duration of the first stage of labor and the greater use of oxytocin among women with a vaginal delivery is consistent with the possibility that greater use of oxytocin may avoid cesarean delivery, but not with observed secular trends in cesarean delivery rates. One would expect that any changes in the threshold for cesarean delivery caused by greater "patience" (allowing a longer duration) and/or "medical management" (greater use of oxytocin) would lead to decreases in cesarean delivery rates.

In summary, evidence suggests that the specific criteria used to define "normal" labor, or a specific threshold for intervention, may affect cesarean delivery rates but not other maternal or neonatal outcomes in some settings. Yet there is no available evidence for the United States. Among women in the United States with spontaneous onset of labor and vaginal delivery, labor progression is slower for women having their first baby compared to women with prior deliveries, but the high proportion of women receiving oxytocin augmentation prevents drawing any inferences about the "normal" labor curve in women with spontaneous onset of labor, no interventions to augment labor, and no adverse maternal or neonatal outcomes.

Research Recommendations

We identified several areas of needed future research:

- It would be extremely useful to have separate labor curves derived from contemporary U.S. data for women with spontaneous onset of labor, no augmentation with oxytocin or other pharmacologic agents, and vaginal delivery of healthy baby, stratified by parity, as well as for women with augmented labor. Such labor curves would provide a better understanding of the modern natural course of labor and may provide better information on when to initiate agents to augment labor and when to proceed with cesarean delivery.
- Evaluation of specific labor management strategies (including the use of partograms) derived from contemporary data sources such as the CSL should be a priority. This evaluation should include comparison of different methods for integrating decision support into existing technologies, such as methods and timing of augmenting labor (oxytocin administration, artificial rupture of the membranes), fetal monitoring, tools to monitor uterine contraction strength and frequency, and the impact of supportive

therapies (massage, fluids, nutrition, positioning) on mode of delivery. This evaluation would help generate best practice recommendations for safe reduction of the primary cesarean delivery rate while balancing maternal and neonatal outcomes.

- Given the importance of the labor process to patient preferences and their birthing experience and the lack of evidence about the impact of available interventions on these preferences, the development of tools for estimating patient preferences for both the process and maternal and neonatal outcomes of labor should be a priority. Discrete choice experiments would be one method appropriate for estimating preferences for these complex tradeoffs.
- Comparison of patient preferences of nulliparous to multiparous women are of great interest as preferences may vary based on prior labor experiences and expectations.
- Studies of these tools/methods should also explore the complexity of decision making that needs incorporate both maternal and paternal preferences, as well as parental preferences as surrogate for infants. Validated measures should be incorporated into clinical trials and prospective studies as specific outcomes.

Conclusions

Dystocia is a common indication for cesarean delivery. Recent data demonstrate that the normal progress of labor with current practice is quite different from curves originally described, although there is still uncertainty about the duration of "normal" labor in the absence of augmentation. Amniotomy and oxytocin decrease duration of labor without increasing cesarean delivery. Emotional support reduces operative delivery rates and patient satisfaction. Further work is needed to identify strategies for management of labor that optimize maternal and neonatal outcomes and patient preferences while minimizing cesarean delivery rates.

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Introduction

Background

Condition

Approximately 80 percent of American women will eventually have at least one child,[1] and the majority of these women will undergo labor. "Labor dystocia" (difficult or obstructed labor)[2] encompasses a variety of concepts, ranging from "abnormally" slow dilation of the cervix or descent of the fetus during active labor[3] to entrapment of the fetal shoulders after delivery of the head ("shoulder dystocia," an obstetric emergency). For the purposes of this systematic review, we assume that "labor dystocia" refers to "abnormal" labor progression during the latent (up to 4-6 cm dilation) or active phases (from 4-6 cm until full dilation) of the first stage of labor, or during the second stage (from complete cervical dilation until delivery of the baby). We also limit our review to women in spontaneous labor and exclude those who are undergoing induced labor.

Prolonged labor may increase the risk for maternal and neonatal infection, fetal distress, neonatal hypoxia, uterine rupture, and postpartum hemorrhage; it may also be a marker for increased risk of maternal pelvic floor and genital trauma during delivery (with a subsequent increased risk for future incontinence and pelvic organ prolapse) and of shoulder dystocia. Reducing the likelihood of these adverse maternal and neonatal outcomes is the underlying rationale for performing a cesarean delivery for the primary indication of labor dystocia.

However, there is a tradeoff, since cesarean delivery itself increases the risk of maternal hemorrhage, venous thromboembolism, and injury to the bladder and other internal organs, and can affect post-delivery mother–baby interactions. Further, having one cesarean delivery increases the likelihood of having subsequent cesarean deliveries.[3] A woman's risk for abnormal placentation (placenta previa or accreta, each of which is associated with significant maternal and neonatal morbidity and mortality) is directly related to the number of prior cesarean deliveries she has had.[4]

Although there is no consensus on the "optimal" cesarean delivery rate (conceptually, the rate that strikes a balance between benefits and harms for both mother and baby that is considered acceptable to most patients), there is widespread consensus that current rates in the United States are too high.[3,5] Strategies to prevent a woman's first, or primary, caesarean delivery may therefore lead to significant improvements in maternal and neonatal outcomes by reducing both the number of primary and repeat cesareans.[3] For this reason, the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) have issued a joint consensus statement aimed at "preventing the first cesarean delivery."[3] Strategies aimed at reducing cesarean delivery for dystocia are a key part of this, since abnormalities of labor progression are the single most common cause of primary cesarean delivery in the United States, accounting for over a third of procedures.[6]

Uncertainty about optimal management of dystocia may play a major role in the well-documented variation in cesarean delivery rates between hospitals that does not appear to be completely attributable to patient characteristics[7] (although other factors not directly related to evidence on comparative effectiveness, such as patient and provider preferences, real or perceived malpractice concerns, and local practice norms may also be important factors). Another source of uncertainty is that there are complex tradeoffs between patient preferences for

the labor and delivery process, on the one hand, and outcomes on the other. These considerations involve issues related to setting (home, birthing center, hospital), provider (lay midwife, nurse-midwife, family physician, obstetrician), and available technology (including analgesia, fetal heart rate monitoring, and measurement of intrauterine pressure).[8-10] There is also wide variety in the maternal and neonatal outcomes that are reported, and the degree to which patient preferences for both process and outcomes is considered.[10-12]

Diagnosis

The effective management of labor dystocia is first dependent on the tool used to diagnose the disorder. In the 1950s, Friedman published his observations on the rate of cervical change among a cohort of women in spontaneous labor[13] and from this constructed labor curves representing the expected rate of cervical change in a population. Deviations from these curves, particularly rates of cervical change slower than expected from the Friedman curve are referred to as protracted or arrest disorders and represent labor dystocia. The Friedman curve has been the primary tool used to diagnose abnormal labor since then, though more recent data from the Consortium on Safe Labor have demonstrated that rates and characteristics of cervical change seen in modern obstetrics are quite different from that represented by the Friedman curve.[14] Identifying what constitutes normal labor is an important initial step in the management of labor dystocia as it first dictates when various treatment options are initiated.

Treatment Strategies

After labor dystocia has been diagnosed, there are a number of strategies for treating abnormal labor that are addressed in this report:

- Use of graphs of cervical dilation versus time ("partograms") to identify patients with slow labor progress, often with an indicator of when intervention is appropriate
- Timing of the artificial rupture of the amniotic membranes (amniotomy) during labor
- Various options for maternal positioning, ambulation, and feeding during labor
- Use of epidural analgesia, or, alternatively, variations in technique (timing, choice of analgesic agents)
- Variations in monitoring labor progress (such as frequency of cervical examination or use of intrauterine pressure catheters) and fetal well-being (fetal heart rate monitoring)
- Variations in strategies for how oxytocin is used during labor augmentation including timing of augmentation relative to labor progress and variation in dosing regimens used
- Variations in strategies for reducing the length of the second stage of labor (after cervical dilation is complete but before the baby has delivered), including different approaches to maternal pushing

The overall goal of treating labor dystocia is to optimize delivery outcomes for mother and child, while attempting to achieve an optimal cesarean delivery rate. As discussed above, the optimal cesarean delivery rate is not known but is the lowest rate that balances benefits and harms to mother and child.

Scope and Key Questions

Scope of the Review

The present review evaluates the comparative effectiveness of different strategies for treating labor dystocia in women with otherwise uncomplicated pregnancies. In addition, one potential source of uncertainty in the available evidence may be variability in the definitions for different phases of labor, and what constitutes "normal" labor across studies and likely in practice as well. The definition of "normal" may vary across different populations and may depend on whether "normality" is based on a specified quantile of the distribution of rates of cervical change in the first stage of labor or rate of fetal descent in the second stage of labor, or on maternal and neonatal outcomes.[15-17] The statistical approach used to define "normality," primarily in reference to rates of cervical change, has also been the source of controversy.[18-20] In order to better understand the impact of this variability on the evidence on specific interventions, we also review the evidence on the definition of "normal" labor progression.

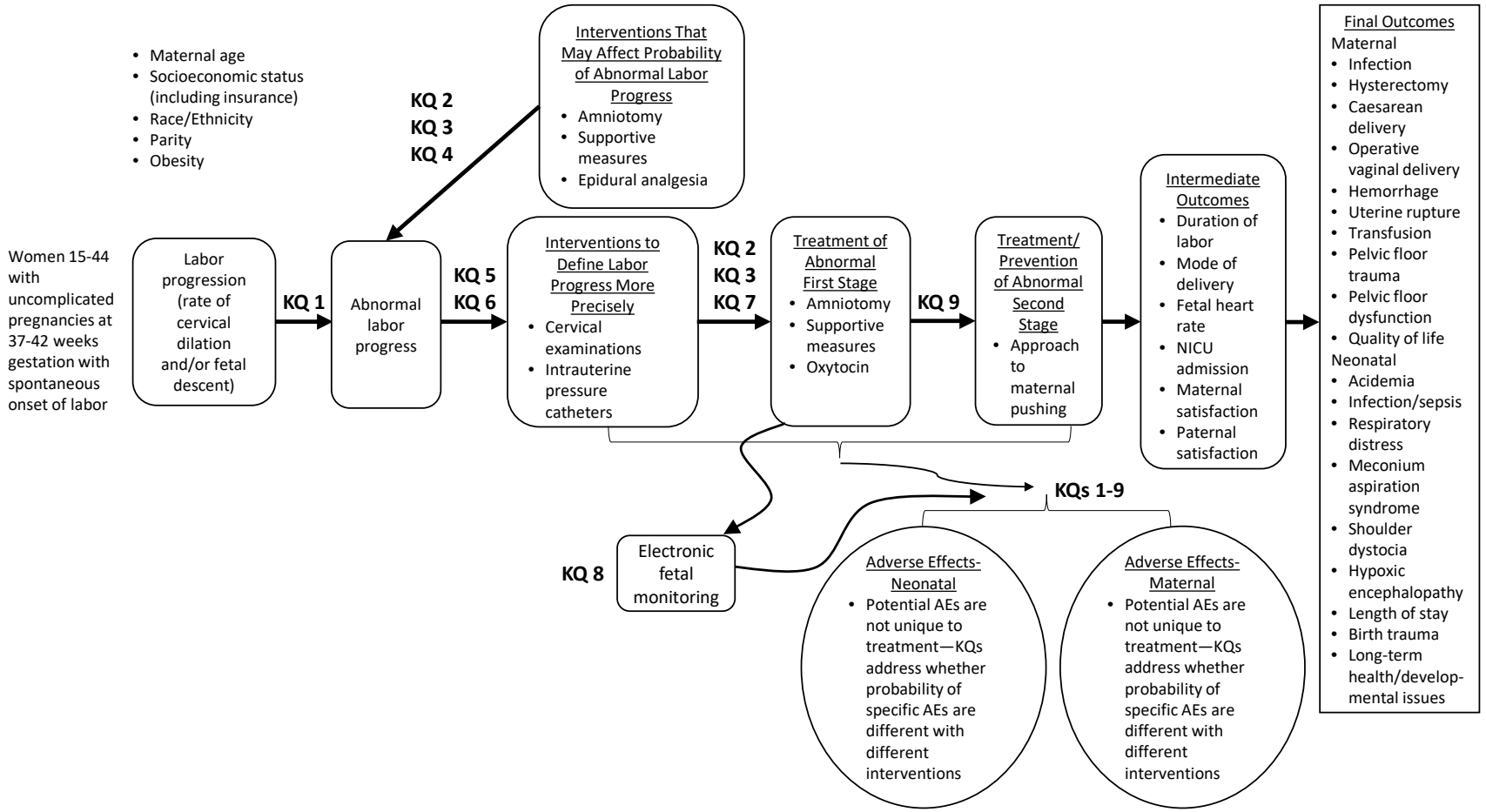
Key Questions

The specific Key Questions (KQs) addressed in this review are listed below, and Figure 1 displays the analytic framework that guided our work.

- KQ 1: Do delivery outcomes for management of abnormal labor differ based on the criteria used to define protracted or arrested labor at different stages of the labor process?
- KQ 2: What are the benefits and harms of amniotomy in women in spontaneous labor?
- KQ 3: What are the benefits and harms of supportive care measures, including ambulation, nutrition, hydration, and emotional support during spontaneous labor?
- KQ 4: What are the benefits and harms of epidural analgesia in labor, particularly in terms of the risk of a diagnosis of prolonged labor?
- KQ 5: How does the frequency of cervical examination affect the probability of specific benefits and harms?
- KQ 6: What are the benefits and harms of intrauterine pressure catheters in the diagnosis and management of labor dystocia?
- KQ 7: For women with abnormal labor, what are the relative benefits and harms of high- versus low-dose oxytocin protocols (including nipple stimulation)?
- KQ 8: For women in spontaneous labor undergoing augmentation with oxytocin, what are the relative benefits and harms (in terms of both maternal and neonatal outcomes) of electronic fetal monitoring versus intermittent auscultation?
- KQ 9: For women in the second stage of labor, is there a benefit from delayed or Valsalva pushing for time to delivery or mode of delivery?

Figure 1 depicts the KQs within the context of the populations, interventions, comparators, outcomes, timings, and settings (PICOTS) considered in this review. It illustrates the progression of spontaneous labor, which may be affected by interventions or management strategies performed prior to the diagnosis of abnormal progression; the criteria used to diagnose abnormal progression; and interventions performed after the diagnosis of abnormal progression.

Figure 1. Analytic framework



Abbreviations: AEs=adverse effects; KQ=Key Question; NICU=neonatal intensive care unit

Organization of This Report

The remainder of the report details our methodology and presents the results of our literature synthesis, with summary tables and strength of evidence grading for major comparisons and outcomes. In the discussion section, we offer our conclusions, summarized findings, and other information that may be relevant to translating this work for clinical practice and future research.

Appendixes provide further details on our methods and the studies we assessed, as follows:

- Appendix A. Exact Search Strings
- Appendix B. Data Abstraction Elements
- Appendix C. List of Included Studies
- Appendix D. List of Excluded Studies
- Appendix E. Key to Included Primary and Companion Articles
- Appendix F. Characteristics of Included Studies
- Appendix G. AMSTAR Quality Assessment for Systematic Reviews
- Appendix H. Risk of Bias Assessment for Included Studies

A list of abbreviations and acronyms is provided at the end of the report.

Methods

The methods for this systematic review (SR) follow the Agency for Healthcare Research and Quality (AHRQ)'s *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* (hereafter referred to as the *Methods Guide*) for the Evidence-based Practice Center (EPC) program[21] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[22] See the review protocol[23] for full details.

Topic Refinement and Review Protocol

The topic of this report and preliminary key questions (KQs) arose through nomination from a professional society and initial development by the Scientific Resource Center (SRC) for AHRQ's Effective Health Care (EHC) program. During the subsequent topic refinement phase, a panel of key informants gave input to the Evidence-based Practice Center (EPC) on the KQs to be examined; these KQs were posted on AHRQ's EHC website for public comment in September 2015 for 3 weeks and revised in response to comments. We then drafted a protocol for the SR and recruited a technical expert panel to provide high-level content and methodological expertise throughout the development of the review. The key informants and technical expert panel represented members of medical professional societies and clinician/researchers in the areas of obstetrics and gynecology, midwifery, and pediatrics; scientific experts; payers; and patients/consumers. The finalized protocol is posted on the EHC website.[23] The PROSPERO registration is CRD42016035567.

Literature Search Strategy

Search Strategy

To identify relevant published literature, we searched PubMed®, Embase®, CINAHL®, and the Cochrane Database of Systematic Reviews (CDSR), limiting the searches to studies published in English from January 1, 2005, to various dates in January 2016 (PubMed and Embase, January 12; CINAHL, January 20; CDSR, January 20). These databases were selected based on internal expert opinion that they would identify most of the relevant literature on this topic and that they reflect the databases used in related SRs, particularly reviews conducted by the Cochrane Pregnancy and Childbirth Group. An experienced search librarian guided all searches. The exact search strings used are given in Appendix A.

We supplemented the electronic searches with a manual search of citations from a set of key primary and review articles.[24-52] The reference lists for identified key articles were manually searched and cross-referenced against our database, and additional relevant articles not already under consideration were retrieved for screening. All citations were imported into an electronic bibliographical database (EndNote® Version X7; Thomson Reuters, Philadelphia, PA). While the draft report is under peer review, we will update the search and include any eligible studies identified either during that search or through peer or public reviews in the final report.

To identify relevant gray literature, the EPC Scientific Resource Center notified stakeholders that the EPC was interested in receiving information relevant to the KQs. We also searched ClinicalTrials.gov for two purposes: (1) to identify relevant articles from completed studies that may not have appeared through other search strategies and (2) as one mechanism to ascertain

publication bias in recent studies. For the latter goal, we sought to identify completed but unpublished studies that could impact the findings of the review. Search terms used for ClinicalTrials.gov are provided in Appendix A We also explored the possibility of publication bias specifically in our quantitative synthesis of the included literature through meta-analysis techniques such as funnel plots when appropriate. Further gray literature assessment included searching the World Health Organization International Clinical Trials Registry Platform search portal and the National Guidelines Clearinghouse to identify potentially relevant study records; we subsequently searched for relevant articles from among the completed studies.

Inclusion and Exclusion Criteria

We specified our inclusion and exclusion criteria based on the PICOTS (populations, interventions, comparators, outcomes, timing, and settings) identified for each question. Table 1 lists inclusion and exclusion criteria.

Table 1. Inclusion and exclusion criteria

PICOTS Element	Inclusion Criteria	Exclusion Criteria
Populations	• KQs 1-5: Women aged 15-44 with uncomplicated pregnancy at 37-42 weeks gestation with a singleton pregnancy with vertex presentation. For the purposes of this review, women who are undergoing induction of labor for any indication are excluded, because the probability of specific outcomes is necessarily different for them. • KQ 6: Women aged 15-44 with uncomplicated pregnancy at 37-42 weeks with suspected abnormalities of the first stage of labor • KQ 7: Women aged 15-44 with uncomplicated pregnancy at 37-42 weeks with a diagnosed abnormality of the first stage of labor • KQ 8: Women aged 15-44 with uncomplicated pregnancy at 37-42 weeks gestation with a diagnosed abnormality of the first stage of labor undergoing augmentation with oxytocin • KQ 9: Women aged 15-44 with uncomplicated pregnancies at 37-42 weeks who have reached complete cervical dilation (with or without augmentation); relevant subgroups include women with and without epidural analgesia • KQs 1-9: Relevant subgroups for all KQs include: (a) maternal age (particularly adolescents and women 35-44 years old); (b) parity; (c) maternal race/ethnicity; (d) maternal socioeconomic status, including insurance status; and (e) maternal obesity.	• Women <15 or >44 years of age • Women in preterm labor • Women undergoing labor induction for any indication • Women with prior history of cesarean delivery • Women with spontaneous rupture of membranes without contractions • KQs 6-8: Studies which do not provide either a definition of “dystocia,” “prolonged labor,” “arrest of labor,” “arrest of descent,” or other relevant diagnosis within the Methods section, or which do not provide a citation with such a definition
Interventions	• KQ 1: Definitions of abnormalities of the latent and active phases of the first stage of labor (up until complete dilation of the cervix) and of the second stage of labor (from complete dilation until delivery of the infant), developed based on data from the Safe Labor Consortium.[3] • KQ 2: Routine amniotomy (artificial rupture of membranes) • KQ 3: Ambulation, routine maternal oxygen	

PICOTS Element	Inclusion Criteria	Exclusion Criteria
	supplementation, specific nutritional recommendations or limitations, specific oral or parenteral hydration recommendations or limitations, continuous emotional support, peanut ball, Lamaze, hypnobirthing, positioning, acupuncture, hydrotherapy, other nonpharmacologic interventions identified through the search • KQ 4: Epidural analgesia • KQ 5: Regular cervical examinations (timing may vary) • KQ 6: Use of internal pressure catheters for measuring timing and strength of uterine contractions • KQ 7: Infusion of low-dose oxytocin • KQ 8: Electronic fetal monitoring (external or internal) • KQ 9: Immediate pushing upon complete dilatation	
Comparators	• KQ 1: Definitions of labor abnormalities based on older data (Friedman Curve)[18,19] • KQ 2: No amniotomy, amniotomy for specific indications (e.g., placement of fetal scalp monitor or intrauterine pressure catheter) • KQ 3: Usual care; interventions above compared to each other • KQ 4: No analgesia, other methods of analgesia (e.g., parenteral narcotics such as morphine or nitrous oxide), nonpharmacologic methods of pain management • KQ 5: Cervical examination only in the setting of clinical concern about labor progress; regular cervical examinations at differing frequencies • KQ 6: External tocodynamometry, no monitoring • KQ 7: High-dose oxytocin; nipple stimulation; maternal oxygen supplementation as an adjunct to oxytocin; different formulations of oxytocin • KQ 8: Intermittent auscultation of fetal heart rate • KQ 9: Other specified maternal techniques/approaches to pushing	
Outcomes	• KQs 1, 3-9: o Maternal • Cesarean delivery • Operative vaginal delivery • Infection (chorioamnionitis, endometritis, wound infection) • Hemorrhage • Uterine rupture • Hysterectomy • Transfusion • Trauma to the pelvic floor (vaginal/perineal/cervical/bladder/rectal injury at the time of delivery) • Pelvic floor dysfunction (long-term urinary or fecal incontinence, fistulae, pelvic organ	For admission to NICU, studies which did not report length of stay if indication distribution was not reported

PICOTS Element	Inclusion Criteria	Exclusion Criteria
	prolapse) • Maternal/paternal experience/satisfaction o Neonatal • Neonatal acidemia (pH<7.1) • Hypoxic encephalopathy • Respiratory distress (need for oxygen supplementation, CPAP, intubation/ventilatory support) • Meconium aspiration syndrome • Neonatal infection/sepsis • Shoulder dystocia • Birth trauma (including brachial plexus injury) • Long-term neonatal health and developmental abnormalities (including cerebral palsy) • Admission to NICU > 24 hours • Neonatal length of stay o Process-related outcomes • Abnormal fetal heart rate tracing • Duration of labor • Mode of delivery (vaginal delivery, assisted vaginal delivery, cesarean delivery) • Parental preferences/satisfaction • KQ 2: o Same as above plus umbilical cord prolapse	
Timing	• KQs 1-9: o Short-term: from beginning of spontaneous labor until discharge home (or equivalent for home delivery) for mother and infant o Long-term: from discharge onwards	
Settings	• KQs 1-9: o Location: hospital, birthing center, home o Providers: obstetrician, family physician, nurse midwife, lay midwife, doula	
Study design	• KQ 1: o Original data, including SRs and MAs o RCTs, prospective and retrospective observational studies with comparator o Observational studies: sample size ≥100 subjects • KQs 2-9: o Original data, including SRs and MAs o RCTs	• Editorials, non-SRs, letters, case series, case reports, abstracts only, retracted/withdrawn articles • Because observational studies with <100 subjects are often underpowered, they were excluded. • SR/MAs were excluded if they did not provide a quantitative summary of results for an outcome of interest

PICOTS Element	Inclusion Criteria	Exclusion Criteria
Publications	• KQs 1-9: o English-language only o Published on or after January 1, 2005 o Relevant methods articles (used for background only)	• Non-English-language publications[a]

[a] Non-English language articles were excluded due to (1) the high volume of literature available in English language publications, (2) the focus of our review on applicability to populations in the United States, and (3) the scope of our KQs.
Abbreviations: CPAP=continuous positive airway pressure; KQ=key question; MA=meta-analyses; NICU=neonatal intensive care unit; PICOTS=populations, interventions, comparators, outcomes, timing, settings; RCT=randomized controlled trial; SR=systematic review

Study Selection

For citations retrieved from PubMed, Embase, CINAHL, and the Cochrane Database of Systematic Reviews, two reviewers independently screened each title and abstract for potential relevance to the KQs using the prespecified inclusion/exclusion criteria described in Table 1. Articles included by either reviewer underwent full-text screening.

At the full-text screening stage, two reviewers independently reviewed the full text of each article and indicated a decision to include or exclude the article for data abstraction. When paired reviewers arrived at different decisions about whether to include or exclude an article, or about the reason for exclusion, we reconciled the difference through review and discussion among investigators. Articles meeting eligibility criteria were included for data abstraction. At random intervals, quality checks were conducted by senior team members to ensure that screening and abstraction were consistent with inclusion/exclusion criteria and abstraction guidelines. We made screening decisions and abstracted data based on the published literature and available online appendices. We did not contact study authors for additional data. All results were tracked using the DistillerSR data synthesis software program (Evidence Partners Inc., Manotick, ON, Canada).

Appendix C provides a list of all articles included for data abstraction. Appendix D provides a list of articles excluded at the full-text screening stage, with reasons for exclusion.

Data Extraction

The research team created data abstraction forms for the KQs that were programmed into DistillerSR software. The abstraction forms were pilot-tested with a sample of included articles to ensure that all relevant data elements were captured and that there was consistency and reproducibility between abstractors. Based on their clinical and methodological expertise, a pair of researchers were assigned to abstract data from each of the eligible articles. One researcher abstracted the data, and the second over-read the article and the accompanying abstraction to check for accuracy and completeness. Disagreements were resolved by consensus or by obtaining a third reviewer's opinion if consensus could not be reached. We linked related publications to avoid duplication of patient cohorts.

We designed the data abstraction forms to collect the data required to evaluate the specified eligibility criteria for inclusion in this review, as well as demographic and other data needed for determining outcomes (intermediate, final, and adverse events outcomes). We paid particular attention to describing the details of the treatment (e.g., frequency of cervical examination, criteria used to diagnose dystocia), patient characteristics (e.g., age, body mass index [BMI],

parity), and study design (e.g., randomized controlled trial [RCT] versus observational) that may be related to outcomes. In addition, we described comparators carefully, as treatment standards may have changed during the period covered by the review. The safety outcomes were framed to help identify adverse events, including those from drug therapies. Data necessary for assessing quality and applicability, as described in the *Methods Guide*,[21] were also abstracted. A complete list of data abstraction elements is provided in Appendix B.

Quality (Risk of Bias) Assessment of Individual Studies

We assessed methodological quality, or risk of bias, for randomized and nonrandomized individual study designs using a components approach, assessing each study for specific aspects of design or conduct (such as allocation concealment for RCTs, or use of methods to address potential confounding), as detailed in AHRQ's *Methods Guide*.[21] Briefly, we rated each study as being of good, fair, or poor quality based on its adherence to well-accepted standard methodologies. For each study, one investigator assigned a summary quality rating, which was then reviewed by a second investigator; disagreements were resolved by consensus or by a third investigator if agreement could not be reached. Table 2 describes the overall study quality assessment ratings. Appendix H presents the risk of bias assessment components for the individual included studies.

Table 2. Definitions of overall quality ratings

Quality Rating	Description
Good (low risk of bias)	These studies had the least bias, and the results were considered valid. These studies adhered to the commonly held concepts of high quality, including the following: a clear description of the population, setting, approaches, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; a low dropout rate; and clear reporting of dropouts.
Fair (moderate risk of bias)	These studies were susceptible to some bias, but not enough to invalidate the results. They did not meet all the criteria required for a rating of good quality because they had some deficiencies, but no flaw was likely to cause major bias. The study may have been missing information, making it difficult to assess limitations and potential problems.
Poor (high risk of bias)	These studies had significant flaws that might have invalidated the results. They had serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

The grading was outcome-specific such that a given study that analyzed its primary outcome well but did an incomplete analysis of a secondary outcome could be assigned a different quality grade for each of the two outcomes. Studies of different designs were graded within the context of their respective designs. Thus, RCTs were graded good, fair, or poor, and observational studies were separately graded good, fair, or poor (Appendix H).

We also rated quality for included SRs. Rating was performed using the AMSTAR tool for assessing the methodological quality of SRs.[53] For each study, one investigator assigned a summary quality rating, a second investigator reviewed the rating; disagreements were resolved by consensus or by a third investigator. Reviews were then assigned overall quality scores according to the following categories[54]:

- Good (low risk of bias)—Systematic reviews that have few or no methodological shortcomings and a low risk of bias.

- Fair (moderate risk of bias)—Systematic reviews that have some methodological flaws but the investigators conclude that the flaws will not seriously bias or invalidate the results.
- Poor (high risk of bias)—Systematic reviews that contain a serious flaw or flaws that, in the judgment of the investigators, are highly likely to bias or invalidate the results.

The AMSTAR quality assessment components for the individual SRs are detailed in Appendix G.

Data Synthesis

We began by summarizing key features of the included studies for each KQ. To the degree that data were available, we abstracted information on study design; patient characteristics; clinical settings; interventions; and intermediate, final, and adverse event outcomes.

We then determined the feasibility of completing a quantitative synthesis (i.e., meta-analysis, decision analysis, or simulation model). For a meta-analysis, feasibility depends on the volume of relevant literature (requiring at least three relevant studies), conceptual homogeneity of the studies (similar intervention comparisons and outcome definitions), completeness of the reporting of results, and the adequacy and completeness of any existing meta-analyses (MAs). Because there are a large number of existing SRs for this topic, particularly from the Cochrane Collaboration, we considered these results using suggested guidance from the *Methods Guide* chapter on integrated bodies of evidence,[55] as outlined in more detail below. As recommended there, we based judgments about the benefit of performing a new quantitative synthesis on an assessment of the existing strength of evidence (using the domains of study limitations, consistency, precision, directness, and reporting bias), and on a judgment about the degree to which a new quantitative synthesis would change conclusions about benefit harm/trade-offs, assessment of strength of evidence, substantially improve the precision of the estimate, or provide a more up-to-date estimate reflecting current practice.

When a meta-analysis was appropriate, we used random-effects models to synthesize the available evidence quantitatively. We tested for heterogeneity using graphical displays and test statistics (Q and I^2 statistics), while recognizing that the ability of statistical methods to detect heterogeneity may be limited. For comparison, we also performed fixed-effect MAs. We present summary estimates, standard errors, and confidence intervals in the Results chapter. We anticipated that intervention effects might be heterogeneous. We hypothesized that the methodological quality of individual studies, study type, characteristics of the comparator, and patients' underlying clinical presentation would be associated with the intervention effects. When there were sufficient studies, we performed subgroup analyses and/or meta-regression analyses to examine these hypotheses. We performed quantitative and qualitative syntheses separately by study type and discuss their consistency qualitatively.

Strength of the Body of Evidence

We graded the strength of evidence for each outcome assessed; thus, the strength of evidence for two separate outcomes in a given study may be graded differently. The strength of evidence was assessed using the approach described in AHRQ's *Methods Guide*.[21,56,57] In brief, the approach requires assessment of five domains: study limitations (previously named risk of bias), consistency, directness, precision, and reporting bias, which includes publication bias, outcome reporting, and analysis reporting bias, as described above. Additional domains used when

appropriate (most relevant to observational studies) were dose-response association, impact of plausible residual confounders, and strength of association (magnitude of effect). When the body of evidence for a particular outcome included both RCTs and observational studies, we graded each study type separately using design-specific criteria. In considering the overall strength of the entire body of evidence, we considered the extent to which the observational evidence is consistent with RCT data, particularly with regard to direction and magnitude of effect. We also explored the consistency of our findings with recent SRs. Because of the risk of unmeasured confounding, observational studies generally do not contribute to estimates of the magnitude of effect, and judgments about the precision of the effect, when RCT data are available. If there are other issues (such as differences in when and where RCTs were performed compared to observational studies, and how these differences might affect applicability), this would generally lead to increased uncertainty about the magnitude and precision of any treatment effect.[58] These domains were considered qualitatively, and a summary rating of high, moderate, or low strength of evidence was assigned for each outcome after discussion by two reviewers. In some cases, high, moderate, or low ratings were impossible or imprudent to make, for example, when no evidence was available or when evidence on the outcome was too weak, sparse, or inconsistent to permit any conclusion to be drawn. In these situations, a grade of "insufficient" was assigned. This four-level rating scale consisted of the following definitions:

- High—We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable, i.e., another study would not change the conclusions.
- Moderate—We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
- Low—We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
- Insufficient—We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.

As noted above, there is already a large body of SRs, some with MAs, in this area. We used the recommendations outlined in the *Methods Guide* chapter on integrating existing SRs in incorporating this body of evidence into our review.[55] Briefly, we confirmed that a given paper was a SR by requiring that the review include an explicit and adequate search, application of predefined eligibility criteria to select studies, risk of bias assessment for included studies, and qualitative or quantitative synthesis of results. Relevance of published reviews meeting these criteria was assessed based on comparability of PICOTS and the extent to which included studies reflect current practice. The quality of relevant existing reviews was graded to determine if the SR was of sufficient quality to inform our evidence base. Key components of this determination included search of multiple sources, use of a generally accepted tool for risk of bias assessment, and sufficient information to assess the strength of the body of evidence that includes the major domains of risk of bias, directness, consistency, precision, and reporting bias (Appendix H). Key

aspects of previous reviews described include number and types of studies included, strength of evidence assessment, and overall qualitative or quantitative findings. Newly identified studies are presented separately from the results of existing reviews. Overall strength of evidence findings are based on the primary evidence, not the quality or number of existing SRs.

Applicability

We assessed applicability across our KQs using the method described in AHRQ's *Methods Guide*.[21,59] In brief, this method uses the PICOTS format as a way to organize information relevant to applicability. The most important issue with respect to applicability is whether the outcomes were different across studies that recruited different populations (e.g., age groups, exclusions for comorbidities) or used different methods to implement the interventions of interest; that is, important characteristics are those that affect baseline (control group) rates of events, intervention group rates of events, or both. We used a checklist applied to each abstracted study to guide the assessment of applicability (Appendix B). For each study, one investigator assigned a summary quality rating, which was then reviewed by a second investigator; disagreements were resolved by consensus or by a third investigator if agreement could not be reached. We then used these data across KQs to evaluate the applicability to clinical practice, paying special attention to study eligibility criteria, demographic features of the enrolled population in comparison to the target population, characteristics of the intervention used in comparison with care models currently in use, the possibility of diagnostic tool or treatment intervention learning curves, and clinical relevance and timing of the outcome measures. We summarized issues of applicability qualitatively.

Peer Review and Public Commentary

Experts in the fields of obstetrics and gynecology, midwifery, pediatrics and neonatology, and methodology, and individuals representing stakeholder and user communities have been invited to provide external peer review of this draft report; AHRQ and an associate editor will also provide comments. The draft report will be posted on the AHRQ website for 4 weeks to elicit public comment. We will address all reviewer comments, revising the text as appropriate, and document the responses in a disposition of comments report that will be made available 3 months after the Agency posts the final report on the EHC website.

Results

Introduction

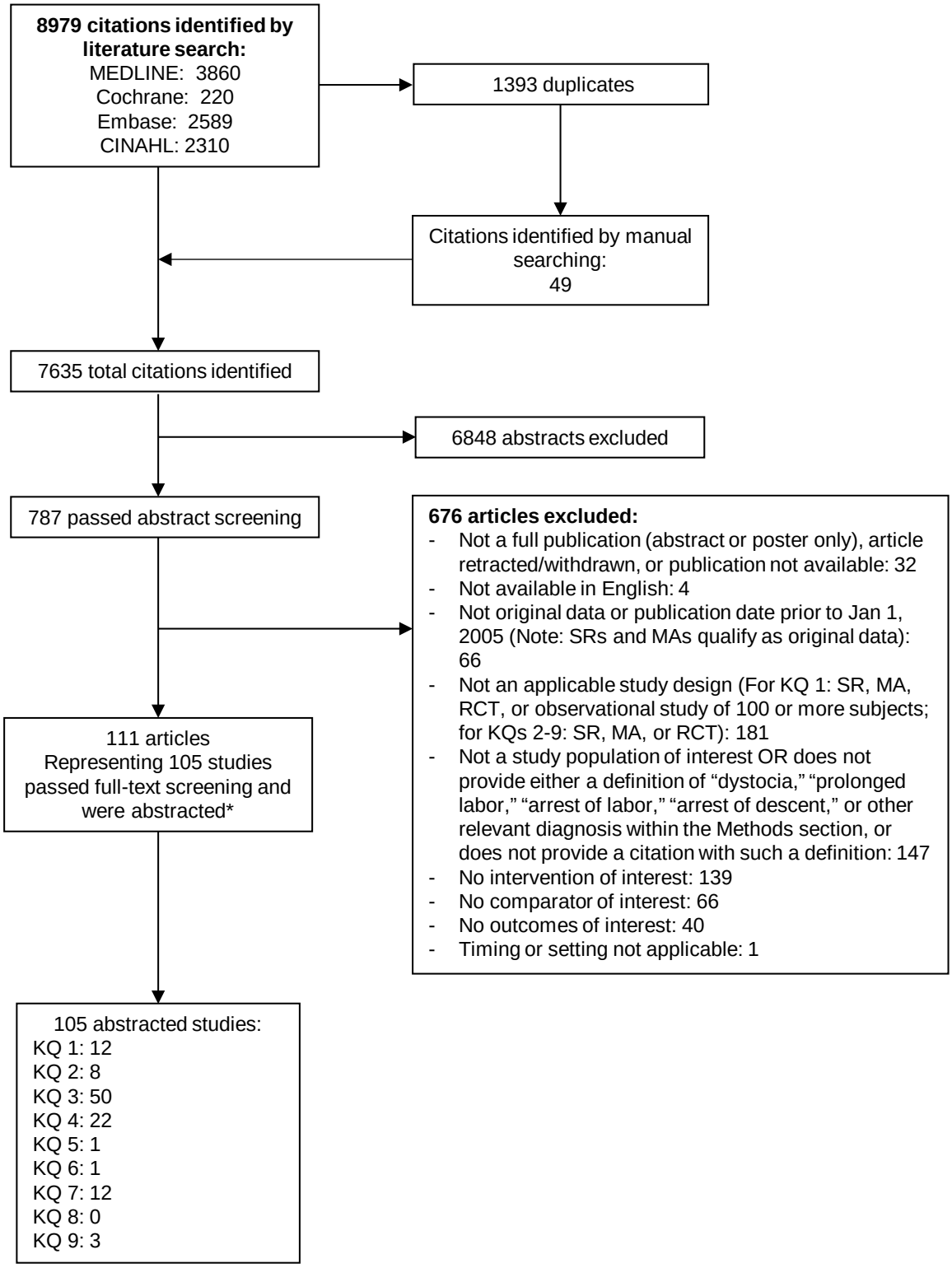
In what follows, we begin by describing the results of our literature searches. We then provide an overall description of the included studies. The remainder of the chapter is organized by key question (KQ). Under each of the nine KQs, we begin with a brief description of the included studies, followed by a bulleted list of the key points of the findings and a detailed synthesis of the evidence. The detailed syntheses are organized first by treatment comparison and then by outcome. We conducted quantitative syntheses where possible, as described in the Methods chapter. Each KQ results section concludes with a summary of the strength of evidence for the main findings.

Results of Literature Searches

Figure 2 depicts the flow of articles through the literature search and screening process. Searches of PubMed, Embase, CINAHL, and the Cochrane Database of Systematic Reviews yielded 8,979 citations, 7,611 of which were unique. Manual searching of gray literature databases and bibliographies of key articles or referral by investigators identified 49 additional citations, for a total of 7,635 citations. No responses were received through public notification to manufacturers of requests for scientific information packets. After applying inclusion/exclusion criteria at the title-and-abstract level, 787 full-text articles were retrieved and screened. Of these, 676 were excluded at the full-text screening stage, leaving 111 articles for data abstraction. These 111 articles described 105 unique studies. The relationship of studies to the review questions is as follows: 12 studies relevant to KQ 1, 8 studies relevant to KQ 2, 50 studies relevant to KQ 3, 22 studies relevant to KQ 4, 1 study relevant to KQ 5, 1 study relevant to KQ 6, 12 studies relevant to KQ 7, 0 studies relevant to KQ 8, and 2 studies relevant to KQ 9 (some studies were relevant to more than one KQ).

Appendix C provides a detailed listing of included articles. Appendix D provides a complete list of articles excluded at the full-text screening stage, with reasons for exclusion. Appendix E provides a “study key” table listing the primary and companion publications for the 105 included studies.

Figure 2. Literature flow diagram



[a] Some studies were relevant to more than one KQ.
Abbreviations: KQ=Key Question; RCT=randomized controlled trial; SR/MA=systematic review/meta-analysis

Description of Included Studies

Overall, we included 105 studies described in 111 publications: 12 studies relevant to KQ 1, 8 studies relevant to KQ 2, 50 studies relevant to KQ 3, 22 studies relevant to KQ 4, 1 study relevant to KQ 5, 1 study relevant to KQ 6, 12 studies relevant to KQ 7, 0 studies relevant to KQ 8, and 2 studies relevant to KQ 9. Of the 105 studies, 83 were RCTs or observational in study design and 23 were SRs. The 82 RCTs/observational studies were conducted wholly or partly in continental Europe or the United Kingdom (UK; 19 studies, 23%), the United States or Canada (15 studies, 18%), the Middle East (24 studies, 29%), Asia (16 studies, 19%), Latin America (6 studies, 7%), and other locations (Africa [2 studies] and Australia/New Zealand [1 study], total 4%). Further details on the studies included for each KQ are provided in the relevant results sections below and in Appendix F.

We searched the ClinicalTrials.gov registry of clinical studies as a mechanism for ascertaining publication bias by identifying studies that have been completed but are as yet unpublished. Among available registries with varying geographic ranges, it is the opinion of the investigators that this widely used, U.S.-based source provided the most relevant information to the populations and interventions of interest in this review. Our search yielded 29 records of completed trials for screening. Manual review identified three of these records as potentially relevant to the KQs. We identified publications (six in total) for all three of these studies, thus finding no indication of publication bias that would impact the results of this review. Five of these publications had been previously identified in our PubMed, Embase, and Cochrane Database of Systematic Reviews searches. The remaining study was a novel publication and was entered into our screening process. Note that we did not compare ClinicalTrials.gov records or protocols listing intended/pre-specified outcomes against published findings.

Key Question 1. Criteria Used to Define Abnormal Labor

KQ 1 was: Do delivery outcomes for management of abnormal labor differ based on the criteria used to define protracted or arrested labor at different stages of the labor process?

This KQ examined whether labor outcomes among women in spontaneous labor differed based on the criteria used to define abnormal labor. In addition, we sought to determine what constitutes normal labor related to rate of cervical change and overall duration of labor.

Description of Included Studies for Criteria Used to Define Abnormal Labor

We identified nine individual studies that examined whether labor outcomes among women in spontaneous labor differed based on the criteria used to define abnormal labor.[16,17,60-66] Of the nine included studies, two were RCTs,[65,66] while seven were observational.[16,17,60-64] Five studies were conducted in the United States,[16,17,60,62,64] two were conducted in Asia,[63,66] and two were conducted in UK/Europe.[61,65] All but one study[66] was conducted in a hospital setting. This lone study was conducted in a maternity home. Six studies reported government funding,[16,17,60,62-64] while three studies were unclear or did not report the funding source.[61,65,66] Five studies were rated as good quality,[17,62,64-66] two as fair quality,[16,61] and two as poor quality.[60,63]

In addition to the above studies, three SRs (2 good quality,[30,67] 1 fair quality[42]) that addressed management of abnormal labor based on certain criteria are also discussed below.

Key Points for Criteria Used to Define Abnormal Labor

Comparisons of pregnancy outcomes based on the criteria used to define abnormal labor

- The use of a 2-hour action line partogram compared with a four-hour action line partogram resulted in shorter total duration of labor (low SOE). Evidence was insufficient regarding rates of cesarean delivery.
- No differences were seen in postpartum hemorrhage rates (moderate SOE), neonatal acidemia rates (low SOE), or vaginal delivery rates (moderate SOE) between women managed with varying partogram strategies.
- Maternal satisfaction was also no different between partogram strategies (low SOE).

What constitutes normal labor?

- Modern labor curves constructed from the Consortium on Safe Labor (CSL) demonstrate significantly different rates of cervical change, duration of labor, and appearance of the curve (absence or presence of an inflection point) between nulliparous and parous women.
- Modern labor curves constructed from the CSL cohort vary significantly from curves constructed from historical cohorts (Friedman or National Collaborative Perinatal Project [NCPP]), with modern curves suggesting a longer duration of the first stage of labor.
- Maternal age influences the duration of the first and second stage of labor among nulliparous women.

Detailed Synthesis

Pregnancy Outcomes Based on the Criteria Used to Define Abnormal Labor

Overview

Two RCTs,[65,66] one observational study,[63] and two good-quality SRs[30,67] compared outcomes among women in spontaneous labor based on the criteria used to define abnormal labor. None of these directly compared outcomes in women whose labor was managed by the Friedman curve versus the Consortium on Safe Labor (CSL) curve.

Partograms

In the 1950s, Friedman published his observations of normal labor through graphical representations of changes in cervical dilation.[13] This work resulted in the use of the Friedman curve as the basis for determining normal labor and the development of partograms.[13,68] A partogram is a graphical representation of a woman's progress in labor. Partograms typically consist of three sections, the first addressing maternal status, the second addressing fetal condition, and the third addressing the progress of labor. The section of the partogram addressing the progress of labor typically contains an alert line which, when crossed, signifies that a woman's rate of cervical change is slower than expected. The initial partograms by Philpott and Castle[68] were constructed with an alert line representing a mean rate of cervical change slower than 10% of the population in the active phase of the first stage of labor.[67] In addition, partograms also include an action line, which initially was positioned 4 hours to the right of the

alert line.[67] The action line serves to help diagnose protracted or arrested labor so that appropriate interventions (e.g., assisted rupture of the membranes, oxytocin augmentation, and/or transfer to a higher level of care) can be administered. The World Health Organization (WHO) developed a partogram that is similar to the Philpott and Castle partogram, with an action line 4 hours to the right of the alert line.[69] In addition, other groups utilize partograms with action lines 2 or 3 hours to the right of the alert line. We identified two good-quality RCTs[65,66] and one good-quality Cochrane review[67] addressing labor outcomes among women managed by partograms. Findings from these studies are summarized in Table 3.

Lavender et al.[65] conducted an RCT at a single site in England comparing outcomes in 2975 nulliparous women managed with a 2-hour action line partogram versus a 4-hour action line partogram. There were no differences in the overall cesarean delivery rate, indication for cesarean delivery, operative vaginal delivery rate, or rates of neonatal acidemia, postpartum hemorrhage, or maternal satisfaction between the two groups. Women managed on the 2-hour action line partogram demonstrated a significantly shorter duration of labor, reported as the time from randomization to delivery. The SOE for duration of labor was reduced given that evidence was from only one RCT in a non-U.S. setting (low SOE).

Fahdhy et al.[66] conducted a randomized trial in Indonesia of births managed in a maternity home with a partogram compared to no partogram; randomization was at the level of the midwife, rather than the patient. The trial included both nulliparous and parous women and results were not stratified by parity. Women managed with the partogram had significantly lower cesarean delivery rates, though no differences were seen in postpartum hemorrhage rates or neonatal resuscitation. The inconsistency between the findings for these two studies for cesarean delivery rates, and the non-U.S. setting resulted in insufficient SOE.

The Cochrane review by Lavender et al.[67] addresses the use of partograms in labor outcomes. This review included 6 studies with 7706 participants and made the following comparisons:

- Partogram versus no partogram
- Partograms with 2-hour versus 4-hour action lines
- Partograms with 2-hour versus 3-hour action lines
- Partograms with 3-hour versus 4-hour action lines
- Partograms with an alert line only versus with both an alert and action line
- Early interventions using a partogram versus late interventions using a partogram

The review planned subgroup analyses by low and high resource setting and did not analyze data by parity. In high-resource settings (not explicitly defined in the review), using the partogram compared with not using the partogram, or use of partograms with different action line durations, did not affect overall cesarean delivery rates or indication for cesarean delivery, except that women being managed using a partogram with a 3-hour action line had higher cesarean delivery rates than women managed using a partogram with a 4-hour action line.[67] In low-resource settings (not explicitly defined in the review), the use of a partogram compared with no partogram resulted in lower overall cesarean delivery rates.[66] Women in low-resource settings managed by a partogram with only an alert line had significantly lower cesarean delivery rates compared to women managed by a partogram with both an alert and action line. Similarly, in women in low-resource settings managed by a partogram, those managed with early intervention versus late interventions had lower cesarean delivery rates. In addition, women in high-resource settings managed with a partogram that contained an assessment of latent phase duration had higher over cesarean delivery rates compared to women managed with a partogram

that did not include an assessment of latent phase duration. This relationship was primarily driven by an increased cesarean delivery rate for the indication of non-reassuring fetal status in women managed by the partogram with a latent phase (Table 3).

The Cochrane review also found that rates of operative vaginal delivery, duration of the first stage of labor, duration of the second stage of labor, rates of neonatal acidemia, maternal infection, or postpartum hemorrhage did not differ based on whether a partogram was used or not, whether the partogram included a 2-hour versus 4-hour action line, a 2-hour versus 3-hour action line, or a 3-hour versus 4-hour action line.[67] Combined with the RCT evidence, these findings resulted in moderate SOE for these outcomes other than acidemia, which had low SOE based on the findings of one RCT.

Table 3. Summary of labor outcomes using partograms

Study Quality Design	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P value	Cesarean: Int	Cesarean: Com	Cesarean: Difference	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Lavender, 2006[65] Good RCT	Partogram 2 hour action line	Partogram 4 hour action line	539.6 (260.3) min	566.4 (289.7) min	0.008	136/1490 (9.1%)	135/1485 (9.1%)	RR 1.0 (0.80 to 1.26)	No	High-resource setting
Fahdhy, 2005[66] Good RCT	Partogram	No partogram	–	–	–	24/322 (4.9%)	15/304 (7.4%)	0.011, OR 0.64 (0.45 to 0.90)	–	Low-resource setting
Lavender, 2013[67] Good SR	Partogram	No partogram	–	–	–	21/224 (9.4%)	52/210 (24.8%)	RR 0.38 (0.24 to 0.61)	–	Low-resource setting
Lavender, 2013[67] Good SR	Partogram	No partogram	First stage: 16.8 (7.3) hr Second stage: 2.4 (1.8) hr	First stage: 16.0 (7.6) hr Second stage: 2.4 (1.9) hr	First stage Mean diff: 0.80 (-0.06, 1.66) Second stage mean diff: 0.0 (-0.21, 0.21)	125/580 (21.5%)	121/576 (21.0%)	RR 1.03 (0.82 to 1.28)	No	High-resource setting
Lavender, 2013[67] Good SR	Partogram	No partogram	–	–	–	146/804 (18.1%)	173/22.0%)	RR 0.64 (0.24 to 1.70)	–	All subjects (both low- and high-resource settings)
Lavender, 2013[67] Good SR	Partogram with Two-hour action line	Partogram with Four-hour action line	–	–	–	Overall: 171/1805 (9.5%) NRFHT: 51/1805 (2.8%) Delay: 120/1805 (6.6%)	Overall: 161/1796 (9.0%) NRFHT: 39/1796 (2.2%) Delay: 122/1796 (6.8%)	Overall: RR 1.06 (0.85 to 1.32) NRFHT: RR 1.30 (0.86 to 1.96) Delay: RR 0.98 (0.77 to 1.25)	–	High-resource setting
Lavender, 2013[67] Good	Partogram with 2-hour action line	Partogram with Three-	–	–	–	Overall: 35/315 (11.1%)	Overall: 43/302 (14.2%)	Overall: RR 0.78 (0.51 to 1.18) NRFHT: RR 0.96 (0.44 to 2.10)	–	High-resource setting

Study Quality Design	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P value	Cesarean: Int	Cesarean: Com	Cesarean: Difference	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
SR		hour action line				NRFHT: 12/315 (3.8%) Delay: 23/315 (7.3%)	NRFHT: 12/302 (4.0%) Delay: 31/302 (10.3%)	Delay: RR 0.71 (0.42 to 1.19)		
Lavender, 2013[67] Good SR	Partogram with 3-hour action line	Partogram with 4-hour action line	–	–	–	Overall: 43/302 (14.2%) NRFHT: 12/302 (4.0%) Delay: 31/302 (10.3%)	Overall: 26/311 (8.4%) NRFHT: 7/311 (2.2%) Delay: 19/311 (6.1%)	Overall: RR 1.70 (1.07 to 2.70) NRFHT: RR 1.77 (0.70 to 4.42) Delay: RR 1.68 (0.97 to 2.91)	–	High-resource setting
Lavender, 2013[67] Good SR	Partogram with Alert line only	Partogram with Alert and Action line	–	–	–	Overall: 55/344 (16.0%)	Overall: 82/350 (23.4%)	Overall: RR 0.68 (0.50 to 0.93)	–	Low-resource setting
Lavender, 2013[67] Good SR	Partogram and Early Intervention	Partogram and Late Intervention	–	–	–	Overall: 55/344 (16.0%)	Overall: 82/350 (23.4%)	Overall: RR 0.68 (0.50 to 0.93)	–	Low-resource setting
Lavender, 2013[67] Good SR	Partogram and Early Intervention	Partogram and Late Intervention	–	–	–	Overall: 171/1490 (11.5%)	Overall: 161/1485 (10.8%)	Overall: RR 1.06 (0.85 to 1.32)	–	High-resource setting
Lavender, 2013[67] Good SR	Partogram and Early Intervention	Partogram and Late Intervention	–	–	–	Overall: 226/2149 (10.5%)	Overall: 243/2146 (11.3%)	Overall: RR 0.94 (0.67 to 1.31)	–	All subjects (both low- and high-resource settings)
Lavender, 2013[67] Good SR	Partogram with latent phase	Partogram without latent phase	–	–	–	Overall: 83/350 (23.7%) NRFHT: 65/350 (18.6%)	Overall: 38/393 (9.7%) NRFHT: 15/393 (3.8%)	Overall: RR 2.45 (1.72 to 3.50) NRFHT: RR 4.87 (2.83 to 8.37) Delay: RR 1.35 (0.59 to 3.08)	–	High-resource setting

Study Quality Design	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P value	Cesarean: Int	Cesarean: Com	Cesarean: Difference	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
						Delay: 12/350 (3.4%)	Delay: 10/393 (2.5%)			

Abbreviations: Com=comparator; Int=intervention; NRFHT=Nonreassuring Fetal Heart Rate Tracing; RCT=randomized controlled trial; RR=relative risk; SR=systematic review

Suzuki Cohort

An observational study conducted in Japan by Suzuki et al.[63] compared duration of the first stage of labor among 2369 nulliparous women having a vaginal delivery following spontaneous labor from 4 sites with published data from the Friedman and CSL cohorts. Women in the Suzuki study had a mean (SD) duration of first stage of labor of 12.3 (7.7) hours compared with 13.3 (7.6) hours in the Friedman data. The CSL data for the duration of the first stage of labor was 7.3 (95% CI 3.3 to 13.7) hours in the CSL datasets. The operative vaginal delivery rates varied significantly between the 3 cohorts (3.5% vs. 51.2% vs. 13.0% in the Suzuki, Friedman, and CSL cohorts, respectively). In addition, the Suzuki study compared the time it took to change from one centimeter dilation to the next centimeter dilation during the first stage of labor to similar data obtained from the CSL study in nulliparous women (Table 4). In both studies, the rate of cervical change increased with advancing cervical dilation, though the rate of change in the Japanese cohort was slower than in the CSL cohort, resulting in a longer duration of the first stage of labor.

Table 4. Time intervals by cervical dilation in nulliparous women, Japanese cohort (Suzuki study) versus CSL (Zhang study)

Cervical dilation, cm	Median (95% CI) time intervals, hours	
	Suzuki study[63]	CSL Zhang study[16]
2-3	7.5 (2.7 to 21.0)	3.2 (0.6 to 15.0)
3-4	6.2 (2.2 to 17.7)	2.7 (0.6 to 10.1)
4-5	4.8 (1.5 to 15.7)	1.7 (0.4 to 6.6)
5-6	3.3 (1.0 to 10.7)	0.8 (0.2 to 3.1)
6-7	2.6 (0.7 to 9.3)	0.6 (0.2 to 2.2)
7-8	1.8 (0.5 to 6.8)	0.5 (0.1 to 1.5)
8-9	1.0 (0.2 to 4.4)	0.4 (0.1 to 1.3)
9-10	0.9 (0.3 to 2.6)	0.4 (0.1 to 1.4)

Abbreviations: CI=confidence interval; CSL=Consortium on Safe Labor

Active Management of Labor

The active management of labor was first described by O'Driscoll and colleagues[70] based on their experience in the National Maternity Hospital in Dublin and was originally designed to allow for a shorter duration of labor and reduce the number of prolonged labors, but more recently it has also been applied to help lower cesarean delivery rates. The originally described active management of labor includes the following interventions: one-to-one nursing support during labor, routine use of amniotomy, intravenous oxytocin, strict diagnosis of labor, strict monitoring of the progress of labor (typically with use of a partogram), strict criteria for the diagnosis of protracted or arrested labor, and peer review of assisted deliveries.[30] We identified one Cochrane Review that addressed the use of a package of care for the active management of labor.[30] The review included 7 studies with 5390 subjects. The authors planned to stratify results by parity, but all of the included studies only included nulliparous women. The overall cesarean delivery rate did not differ between women receiving active management of labor and women receiving usual care when all studies were included. In 1 of the 7 studies, approximately one-third of the subjects were excluded post-randomization, as randomization occurred at 30 weeks and many women developed reasons for exclusion following this.[71] In sensitivity analysis that excluded this study, active management of labor resulted in significantly lower cesarean delivery

rates and shorter duration of labor when compared with usual care (Table 5).[30] Active management of labor was also associated with shorter duration of time from admission to delivery and the first stage of labor compared to usual care. The second stage of labor was not different between the two groups (Table 5). Active management of labor did not affect rates of operative vaginal delivery, postpartum hemorrhage, maternal satisfaction, or maternal infection.

Table 5. Labor outcomes by active management of labor

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: Difference	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Brown, 2013[30] Good	Active management of labor	Routine care	–	–	–	Overall: 343/2573 (13.3%)	Overall: 416/2817 (14.8%)	Overall: RR 0.88 (0.77 to 1.01)	–	All studies including 1 with high number of post-randomization exclusions
Brown, 2013[30] Good	Active management of labor	Routine care	Admission to delivery: 7.7 (1.9) hr First stage: 6.8 (2.3) hr Second stage: 0.86 (0.43) hr	Admission to delivery: 9.4 (1.7) hr First stage: 8.3 (1.9) hr Second stage: 0.89 (0.44) hr	Difference in admission to delivery: -1.69 (-2.08, -1.31) hr Difference in first stage: -1.56 (-2.17, -0.96) hr Difference in second stage: -0.02 (-0.06, 0.02) hr	Overall: 146/1564 (9.3%)	Overall: 240/1911 (12.5%)	Overall: RR 0.77 (0.63 to 0.94)	Yes	Sensitivity analysis with 1 study excluded (high-post randomization exclusion rate)

Abbreviations: Com=comparator; hr=hour; Int=intervention; RR=relative risk

What Constitutes Normal Duration of Labor?

Overview

Five observational studies[16,17,60,62,64] and one fair-quality SR/MA[42] addressed the question of what constitutes normal duration of labor. The populations studied varied based on parity and whether labor was augmented, both of which may affect the duration of labor.

National Collaborative Perinatal Project and the Consortium on Safe Labor

The National Collaborative Perinatal Project (NCPP) and the CSL were two large observational studies that both addressed duration of labor. The NCPP was a large observational study conducted at 12 sites between 1959 and 1966 and included 54,304 singleton pregnancies that delivered at 20 weeks or later.[17] Of these, labor outcomes were reported for 26,838 parturients with singleton gestation, spontaneous onset of labor, and who completed the first stage of labor.[17] In contrast, the CSL was a large observational study conducted at 19 sites between 2002 and 2008, with 87 percent of the births occurring between 2005 and 2007.[16] The CSL included 62,415 subjects who had spontaneous onset of labor and a vaginal delivery. The rate of labor augmentation differed significantly between the two cohorts. Within the NCPP cohort, 14.6 percent of women received oxytocin augmentation (20% of nulliparous, 12% of parous 1, and 12% or parous 2+),[17] while 45.9 percent of women in the CSL cohort received oxytocin augmentation (47% of nulliparous, 45% of parous 1, and 45% of parous 2+).[16]

Unlike the nulliparous labor curve of Friedman, which demonstrates a clear inflection point at which the rate of cervical dilation changes dramatically (transition from latent to active phase of labor) during the course of the first stage of labor, neither the NCPP or CSL nulliparous labor curves demonstrate a clear inflection point at which the rate of cervical dilation changes.[13,14,16,17] In contrast, the labor curves for multiparous women in both the NCPP and CSL cohorts demonstrate an inflection point at which the rate of cervical dilation changes. In the NCPP cohort, the inflection point for Parous 1 women occurred at 5.5 cm, while for Parous 2+ women, the inflection point occurred at 5 cm dilation.[17] In the CSL cohort, the inflection point occurred at 6 cm cervical dilation for both Parous 1 and Parous 2+ women.[16] There were significant differences in maternal age, race/ethnicity, BMI, cervical dilation at admission, and rate of oxytocin augmentation between the two cohorts. The extent to which differences in these patient characteristics contributed to the observed differences in labor curves is unclear.

The NCPP and CSL datasets both reported the time it took to change from one centimeter dilation to the next centimeter dilation during the first stage of labor (Table 6).

Table 6. Time intervals by cervical dilation and parity, NCPP and CSL cohorts

Cervical dilation, cm	Median (95th percentile) time intervals, hours					
	NCPP cohort[17]			CSL cohort[16]		
	Parity 0	Parity 1	Parity 2+	Parity 0	Parity 1	Parity 2+
3-4	1.2 (6.6)	–	–	1.8 (8.1)	–	–
4-5	0.9 (4.5)	0.7 (3.3)	0.7 (3.5)	1.3 (6.4)	1.4 (7.3)	1.4 (7.0)
5-6	0.6 (2.6)	0.4 (1.6)	0.4 (1.6)	0.8 (3.2)	0.8 (3.4)	0.8 (3.4)
6-7	0.5 (1.8)	0.4 (1.2)	0.3 (1.2)	0.6 (2.2)	0.5 (1.9)	0.5 (1.8)
7-8	0.4 (1.4)	0.3 (0.8)	0.3 (0.7)	0.5 (1.6)	0.4 (1.3)	0.4 (1.2)
8-9	0.4 (1.3)	0.3 (0.7)	0.2 (0.6)	0.5 (1.4)	0.3 (1.0)	0.3 (0.9)
9-10	0.4 (1.2)	0.2 (0.5)	0.2 (0.5)	0.5 (1.8)	0.3 (0.9)	0.3 (0.8)

Abbreviations: cm=centimeter; CSL=Consortium on Safe Labor; NCPP=National Collaborative Perinatal Project

The time from admission to 10 cm cervical dilation differed within each cohort based on the cervical dilation at the time of admission. The median (95th percentile) time from admission to delivery within the NCPP cohort was 6.3 (20.7), 4.5 (16.2), 3.2 (14.2), and 2.1 (9.3) hours for women admitted at 2-2.5 cm, 3-3.5 cm, 4-4.5 cm, and 5-5.5 cm cervical dilation, respectively.[17] For women in the CSL cohort, the median (95% percentile) time from admission to delivery was 8.4 (20.0), 6.9 (17.4), 5.3 (16.4), and 3.8 (12.7) hours for women admitted at 2-2.5 cm, 3-3.5 cm, 4-4.5 cm, and 5-5.5 cm cervical dilation, respectively.[16]

Frigo Italian Cohort

Frigo et al.[61] conducted a cohort study of nulliparous women in spontaneous labor who delivered vaginally to determine the duration of the first stage and second stage of labor, with the ultimate goal of constructing labor curves for their population and then comparing those curves to the curves published by Friedman and the CSL. All women in the Frigo cohort received regional analgesia and were assigned in an alternating fashion to combined spinal plus epidural analgesia or to epidural analgesia alone. The mean duration of the first stage of labor in their population was 4 hours and 30 minutes (SD 1.52 hours), and the mean duration of the second stage of labor was 1 hour and 10 minutes (SD 0.43 hours). Oxytocin augmentation was received in 55.9 percent of the study population. Within this cohort, women with combined spinal plus epidural analgesia had significantly shorter mean (SD) duration of the first (4.01 [1.43] vs. 4.60 [1.39] hours, p=0.043) and second (1.05 [0.38] vs. 1.15 [0.35] hours, p=0.036) stages of labor compared to women receiving epidural analgesia alone (Table 7).

Table 7. Duration of labor and oxytocin augmentation in the Frigo, Friedman, and CSL cohorts

Outcome	Frigo cohort[61]	Friedman cohort[14]	CSL cohort[16]
Duration of first stage, hours	4.30	4.35	5.50
Duration of second stage, hours	1.10	0.39	0.53
Oxytocin augmentation, % of study population	55.9	50	45.9

Abbreviation: CSL=Consortium on Safe Labor

Labor Outcomes by Duration of Labor and Maternal Age

A large, single-center observational study[62] of 10,661 nulliparous women in spontaneous labor assessed delivery outcomes based on the duration of labor. The duration of the first stage of labor was divided into 3 categories: <5th percentile, 5th to 95th percentile, and >95th percentile. Mode of delivery and rates of postpartum hemorrhage, chorioamnionitis, and endometritis varied by duration of the first stage of labor (Table 8). The incidence of third or fourth degree perineal laceration, neonatal acidemia, neonatal sepsis, shoulder dystocia, or birth trauma was not influenced by duration of the first stage of labor. In multivariable analysis, mode of delivery (overall adjusted odds ratio [aOR] 0.62 [95% CI, 0.45 to 0.84] for cesarean delivery and aOR 2.28 [95% CI, 1.92 to 2.72] for first stage duration for the <5th percentile and >95th percentile compared to the 5th to 95th percentile, respectively) and chorioamnionitis (aOR 0.31 [95% CI, 0.17 to 0.56] and aOR 1.58 [95% CI, 1.25 to 1.98] for first stage duration for the <5th percentile and >95th percentile compared to the 5th to 95th percentile, respectively) remained significantly different based on duration of the first stage of labor.

Table 8. Maternal outcomes by duration of the first stage of labor

Outcome	<5th percentile (0-2.8 hours) n=525	5th to 95th percentile (2.8-30 hours) n=9611	>95th percentile (>30 hours) n=525	P Value
Mode of delivery, %				
Spontaneous vaginal	80.6	72.9	63.8	<0.001
Operative vaginal	17.4	21.0	22.6	<0.001
Cesarean	2.0	6.1	13.5	<0.001
Postpartum hemorrhage, %	8.6	9.8	14.0	0.004
Chorioamnionitis, %	2.9	12.5	23.5	<0.001
Endometritis, %	1.0	2.4	3.2	0.04

The duration of labor is affected by maternal age. A single-center observational study of 31,976 women demonstrated that the duration of the first and second stage of labor is associated with maternal age.[64] In multivariable analysis including only those women in spontaneous labor (excludes women who were induced), older nulliparous women demonstrated significantly longer first stage of labor compared to younger women, though this relationship was not seen among multiparous women. Older nulliparous and multiparous women had longer adjusted duration of the second stage of labor compared to younger women (Table 9).

Table 9. Duration of labor (minutes) by maternal age

Parity and stage of labor	<20 yrs	20-24 yrs	25-29 yrs	30-34 yrs	35-39 yrs	≥40 yrs
Nulliparous						
First stage	550 (170 to 1400)	555 (170 to 1423)	595 (180 to 1445)	630 (180 to 1590)	660 (180 to 1734)	585 (200 to 1740)
Second stage	51 (10 to 232)	65 (12 to 245)	89 (15 to 282)	118 (19 to 317)	127 (21 to 336)	148 (21 to 381)
Multiparous						
First stage	368 (117 to 1080)	365 (103 to 1080)	355 (95 to 1075)	345 (90 to 1080)	345 (90 to 1110)	343 (80 to 1098)
Second stage	16 (3 to 120)	15 (3 to 128)	18 (3 to 160)	20 (3 to 191)	24 (4 to 221)	26 (3 to 197)

Notes: Data are median duration of labor (95% CI) in minutes. Includes women who were induced (range 12.7 to 19.7%).
Abbreviations: yrs=years

Labor Duration by Initial Rate of Cervical Change at Admission

An observational study of 216 nulliparous women compared the duration of labor and mode of delivery based on the initial rate of cervical change at the time of admission.[60] Women with an initial rate of cervical change of <0.5 cm per hour in the first 4 hours were defined as being in pre-labor, and women with an initial rate of cervical change of >0.5 cm per hour were defined as being in active labor. Women in active labor were less likely to be delivered by cesarean deliver and had shorter duration of labor from admission to 10 cm compared to women in admitted in pre-labor.

A fair-quality SR of 18 studies including 7009 nulliparous women by the same lead author[42] demonstrated that the mean (SD) duration of the active phase of labor in nulliparous women was 6.0 (2.0) hours, with an associated mean (SD) rate of cervical change of 1.2 (0.5) cm per hour.

Strength of Evidence for Criteria Used to Define Abnormal Labor

Table 10 summarizes the SOE for the use of partograms described above. In general, the SOE was reduced for outcomes because the evidence was based on evidence from non-U.S. settings (and several focused on low-resource settings).

Table 10. Partogram use: Strength of evidence for major outcomes and adverse events

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	1 RCT[65] (2,975)	**Improvement with 2-hour action line partogram:** An RCT in the UK demonstrated a shorter total duration of labor in women managed with a 2-hour action line partogram compared to women managed with a 4-hour action line partogram.	Low (Indirect [non-U.S. setting], 1 study)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[65,66] (3,601) 1 SR/MA[67] (7,706)	**Inconclusive:** Inconsistent findings from 2 studies combined with non-U.S. settings resulted in insufficient SOE. Systematic review evidence also was inconsistent between low and high-resource settings.	Insufficient (Indirect [non-U.S. setting], Inconsistent)
Process Related Outcomes – Operative Vaginal Delivery	1 RCT[65] (1,929) 1 SR/MA[67] (7,706)	**No difference:** No difference in operative vaginal delivery rates between women managed with varying partogram strategies.	Moderate (non-U.S. setting)
Process Related Outcomes – Parental Preferences	1 RCT[65] (1,929)	**No difference:** An RCT in the UK demonstrated no difference in maternal satisfaction scores between women managed with a two-hour action line partogram compared to women managed with a four-hour action line partogram.	Low (non-U.S. setting, 1 study)
Adverse Events			
Maternal Outcomes – Hemorrhage	2 RCTs[65,66] (3,601)	**No difference:** No difference postpartum hemorrhage rates among women managed with varying partogram strategies.	Moderate (non-U.S. setting)
Neonatal Outcomes – Respiratory Distress	1 RCT[66] (626)	**Inconclusive:** SOE was rated as insufficient given findings from 1 study in non-U.S. low resource setting.	Insufficient (non-U.S. setting, 1 small study)
Neonatal Outcomes – Acidemia	1 RCT[65] (1,929)	**No difference:** No difference in neonatal acidemia rates between women managed with varying partogram strategies.	Low (non-U.S. setting, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SR/MA=systematic review/meta-analysis

Key Question 2. Amniotomy

KQ 2 was: What are the benefits and harms of amniotomy in women in spontaneous labor?

Description of Included Studies

We identified six RCTs that examined the benefits and harms of amniotomy (± oxytocin) in women in spontaneous labor.[72-77]. Of these, four studies were conducted in the Middle East,[72-74,77] one was conducted in Asia,[76] and one was conducted in Africa.[75] All but one study[77] were conducted in a hospital setting. The lone exception was a study conducted in an obstetrics and

gynecology unit. All six studies were unclear about or did not report their funding source. Four studies were rated as good quality,[73-76] and two studies were rated as fair quality.[72,77]

Comparisons of interest were amniotomy versus an alternative control treatment without amniotomy (five studies[72-75,77]) and amniotomy plus oxytocin versus control treatment (two studies[73,76]).

In terms of parity, three studies reported results for nulliparous women only;[72,76,77] one reported results for nulliparous and multiparous women separately (with no analysis of combined results);[74] one reported results for nulliparous and multiparous women combined and for each of the parity subgroups;[73] and one reported results for women of unspecified parity.[75]We were able to combine results across parity subgroups for some dichotomous outcomes of interest; we report those below.

In addition to the above studies, three good-quality SRs addressed the benefits and harms of amniotomy.[30,78,79] All three SR/MAs examined the role of amniotomy, with or without oxytocin, to prevent labor dystocia,[78] shorten spontaneous labor,[79] or prevent cesarean delivery[30] in spontaneous labor. Wei et al. performed a meta-analysis to estimate the effects of amniotomy plus oxytocin for prevention of, or therapy for, delay in labor progress on the cesarean delivery rate and on indicators of maternal and neonatal morbidity. Smyth et al.[79] compared amniotomy alone to intention to preserve the membranes to shorten the duration of labor. The primary objective of the analysis performed by Brown et al.[30] was to determine whether a predefined package of interventions during childbirth such as "active management of labor" reduces the cesarean delivery rate in low-risk women and improves women's satisfaction. Several of the studies included in our review overlapped with studies included in these three reviews.

Key Points for Amniotomy

Amniotomy versus control treatment

- Amniotomy decreases the total duration of labor in nulliparous women (moderate SOE).
- There were no differences in rates of maternal infection, hemorrhage, or trauma to the pelvic floor (moderate SOE) for early amniotomy versus control.

Amniotomy plus oxytocin versus control treatment

- Routine amniotomy plus oxytocin decrease the duration of labor and has a similar effect in both nulliparous and multiparous women (high SOE).
- Routine amniotomy plus oxytocin do not differ compared to control treatment in cesarean delivery rates in both nulliparous and multiparous women (high SOE).

Detailed Synthesis for Amniotomy

Amniotomy versus Control Treatment

Amniotomy is the practice of rupturing the amniotic sac during the course of labor and may be performed for a variety of indications. For the purpose of preventing labor dystocia, amniotomy is performed early in the labor process although the optimal timing is an area of active debate. Across included studies, amniotomy has been compared to various control treatments. The specific control treatment was described across all studies as care according to

the obstetric providers' discretion without intentional amniotomy in the absence of other indications (such as direct monitoring of fetal heart rate or intrauterine pressure).

Results in Nulliparous Women

Four RCTs examined amniotomy versus control treatment in nulliparous women.[72-74,77]

Duration of Labor and Cesarean Delivery Rates

All four trials demonstrated a statistically significant decrease in the total duration of labor in women randomized to amniotomy (moderate SOE) (Table 11). One fair-quality trial[72] also demonstrated a significantly decreased cesarean delivery rate in women randomized to amniotomy. The remaining three studies, showed no significant differences in cesarean delivery rates between groups. The SOE was rated as insufficient given inconsistent and imprecise findings.

Table 11. Amniotomy versus control in nulliparous women—total duration of labor and cesarean delivery rates

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Abdullah, 2010[77] Fair	Routine amniotomy N=100	Amniotomy for specific indications N=100	399.6 min ±84.6	456 min ±104.4	<0.001	8 (8%)	10 (10%)	0.62	No	Duration of labor defined as time from enrollment to delivery
Ghafarzadeh, 2015[72] Fair	Routine amniotomy at <4 cm N=150	Amniotomy for specific indications N=150	450 min ±42	504 min ±60	<0.001	17 (11.3%)	59 (39.3%)	<0.0001 aOR 0.183 (95% CI, 0.099 to 0.338) – *adjusted for BMI, age, gestational age, neonatal weight, cervical dilation, cervical effacement*	Yes	Duration of labor defined as onset of uterine contractions until 1 hr after expulsion of placenta
Mikki, 2007[74] Good	Amniotomy shortly after admission N=74	Routine care/ amniotomy if indicated N=83	231 min ±110	291 min ±138	<0.001	–	–	Unadjusted OR 0.52 (95% CI 0.12 to 2.2); p=0.48	No	Duration of labor defined as time from randomization to full dilation
Nachum, 2010[73] Good	Amniotomy N=21	No intervention N=23	629 min ±338	740 min ±294	0.25	2 (9.5%)	0 (0%)	0.22	–	Duration of labor defined as time from enrollment until delivery

Abbreviations: aOR=adjusted odds ratio; Com=comparator; CI=confidence interval; cm=centimeter; hr=hour; Int=intervention; min=minute; N=number; OR=odds ratio

Maternal Outcomes after Amniotomy

In two good quality RCTs, there was no evidence of increased risk of infection or maternal hemorrhage associated with amniotomy (moderate SOE).[73,74] In one good quality RCT comparing amniotomy shortly after admission (N=74) to control treatment (N=83), there were no cases of maternal fever in the intervention group, and 1 case (1.2%) of maternal fever in the control group. There was 1 case of postpartum hemorrhage in the intervention group (1.4%) compared to 2 cases in the comparator group (2.4%).[74]

In another good quality RCT, comparing amniotomy (N=21) to unrandomized women whose labor progressed spontaneously without intervention (N=23), there were 3 cases (14%) of intrapartum fever/antibiotic use in the intervention group, as compared with 0 cases (0%) in the control group (p=0.10). There were no cases of postpartum hemorrhage in either group.[73]

Three good-quality studies described trauma to the pelvic floor, as outlined in Table 12 below. There was no evidence of increased risk of pelvic floor trauma in either group (moderate SOE).

Table 12. Amniotomy versus control in nulliparous women—trauma to the pelvic floor

Study Quality	Intervention	Comparator	Specific Outcome	Results Intervention	Results Comparator	P Value
Abdullah, 2010[77] Fair	Amniotomy N=100	Amniotomy for specific indications N=100	Episiotomy	53 (53%)	61 (61%)	0.25
Mikki, 2007[74] Good	Amniotomy shortly after admission N=74	Routine care/ amniotomy if indicated N=83	Episiotomy	54 (74.0%)	59 (72.0%)	0.78
Mikki, 2007[74] Good	Amniotomy shortly after admission N=74	Routine care/ amniotomy if indicated N=83	Tears (not further specified)	11 (15.1%)	19 (22.9%)	0.21
Nachum, 2010[73] Good	Amniotomy N=21	No intervention N=23	Anal sphincter tear	0 (0%)	0 (0%)	NS

Abbreviations: NS=not significant

Neonatal Outcomes after Amniotomy

In one good quality RCT comparing amniotomy shortly after admission (N=74) to control treatment (N=83),[74] there were no cases of neonatal fever in either group (low SOE).

Process-Related Outcomes after Amniotomy

In a small good quality RCT, comparing amniotomy (N=21) to control treatment (N=23) maternal satisfaction was reported by patients on a scale of 1-5. Women randomized to amniotomy reported a lower average maternal satisfaction score (4.4 ± 0.9), compared to control treatment (5.0 ± 0.2) (insufficient SOE).[73]

Results in Multiparous Women for Amniotomy

Two good-quality RCTs compared amniotomy to control treatment in multiparous women.[73,74]

Duration of Labor and Cesarean Delivery Rates for Amniotomy

One study demonstrated a decreased total duration of labor in multiparous women randomized to amniotomy versus control treatment. A second good quality study did not demonstrate this difference (insufficient SOE). There was no difference in cesarean delivery rates between groups in the second study (insufficient SOE).

The first study was a good quality RCT, comparing amniotomy (N=266) to control treatment (N=267) in multiparous women, there was a significantly decreased total duration of labor in the intervention group (133 ± 71 minutes) as compared with the comparison group (172 ± 106 minutes) ($p < 0.001$).[74] Rates of cesarean delivery were not reported for this study.

The second good quality RCT, compared amniotomy (N=49) to unrandomized women whose labor progressed spontaneously without intervention (N=47) in multiparous women, there was no difference in the total duration of labor in the intervention group (352 ± 320 minutes) as compared with the comparison group (376 ± 232 minutes; $p=0.67$). The rate of cesarean was similar in both groups in this study. There were no cesarean deliveries in the intervention group, and 1 cesarean delivery in the intervention group (2%).[73]

Maternal Outcomes after Amniotomy

In two good quality RCTs, there was no evidence of increased risk of infection, maternal hemorrhage or pelvic floor trauma associated with amniotomy as compared with control treatment in multiparous women (moderate SOE).[73,74]

In one good quality RCT comparing amniotomy shortly after admission (N=266) to control treatment (N=267) in multiparous women, there was 1 case (0.4%) of maternal fever in the intervention group, and 0 cases (0%) in the control group. There were 2 cases (0.7%) of postpartum hemorrhage in the intervention group and 2 cases (0.7%) in the comparison group. In regards to pelvic floor trauma, there were 8 cases of episiotomy (3.0%) in the intervention group and 14 cases of comparison group (5.3%). Lacerations were reported in 29.0% of women in the intervention group and in 33.7% of women in the comparison group.[74]

In another good quality RCT, comparing amniotomy (N=49) to unrandomized women whose labor progressed spontaneously without intervention (N=47) in multiparous women, there was 1 case (2%) of maternal fever/antibiotic use in the intervention group, as compared with 0 cases (0%) in the control group. There were no cases of postpartum hemorrhage in either group. Pelvic floor trauma was reported as rates of anal sphincter tear. There were no cases of anal sphincter tear reported in either group.[73]

Neonatal Outcomes after Amniotomy

In one good quality RCT comparing amniotomy shortly after admission (N=266) to control treatment (N=267) in multiparous women, there were no cases of neonatal fever in the intervention group (0%) and 1 case (0.4%) in the comparison group.[74]

Process-Related Outcomes after Amniotomy

In a good quality RCT, comparing amniotomy (N=49) to control treatment (N=47) maternal satisfaction was reported by multiparous women on a scale of 1-5. Multiparous women randomized to amniotomy reported a similar average score (4.9 ± 0.4) as compared to control treatment (5.0 ± 0.0; $p=0.087$).[73]

Results in Women of Mixed or Unspecified Parity for Amniotomy

Two good-quality RCTs compared amniotomy to control treatment in women of unspecified[75] or mixed[73] parity. In addition, we combined nulliparous and multiparous results (reported separately, without a combined analysis), where possible, for dichotomous outcomes from a third good-quality trial.[74]

Duration of Labor and Cesarean Delivery Rates for Amniotomy

One RCT reported outcomes for a group of women of unspecified parity.[75] Low-risk women who presented in labor were randomized to amniotomy (n=58) versus control treatment (n=59). In this study, control treatment was defined as monitoring with a partogram until delivery, with labor augmentation if progress was not considered satisfactory. Augmentation consisted of the use of intravenous oxytocin infusion in the control group, and amniotomy was considered after 1 hour or more. Mean total duration of labor (± SD) was significantly shorter in women randomized to amniotomy (208.27 ± 22.52 minutes) versus control treatment (292.07 ± 23.41 minutes; $p<0.05$). There was also a statistically significant ($p<0.05$) decrease in the duration of the first stage of labor (randomization to full cervical dilation) in the intervention group (mean 182.17 ± SD 19.70 minutes) versus controls (mean 265.02 ± SD 20.40 minutes). There was no significant difference in the duration of the second stage of labor. There was no significant difference in cesarean delivery rates between the two groups (1.5% in both).

A second RCT[73] examined delivery outcomes in women who were randomized to amniotomy (n=70) as compared to a control group (n=70). In this case, the control group was composed of unrandomized women whose labor progressed spontaneously without intervention. Results were reported for nulliparous and multiparous women combined and for each of the parity subgroups. For the combined population, there were no significant differences between treatment groups in total duration of labor. Mean total duration of labor (± SD) was 431 ± 346 minutes in women randomized to amniotomy. Mean total duration of labor (± SD) was 498 ± 306 minutes in women randomized to control ($p=0.23$). There was no significant difference in cesarean rate between treatment groups (intervention 2.8%, control 1.4%) (low SOE).

Maternal Outcomes after Amniotomy

In two good quality RCTs, there was no significant increased risk of infection, maternal hemorrhage, or pelvic floor trauma associated with amniotomy as compared with control treatment in a mixed group (multiparous and nulliparous) of women.[73,74] SOE was moderate for all three outcomes.

In one good quality RCT comparing amniotomy shortly after admission (N=340) to control treatment (N=350) in nulliparous and multiparous women, there was 1 case (0.3%) of maternal fever in the intervention group, and 1 case (0.3%) in the control group. There were 3 cases (0.9%) of postpartum hemorrhage in the intervention group and 4 cases (1.1%) in the comparison group. In regards to pelvic floor trauma, there were 62 cases of episiotomy (18.2%) in the intervention group and 72 cases (20.9%) in the comparison group. Lacerations were reported in 25.9% of women in the intervention group and in 31.1% of women in the comparison group.[74]

In another good quality RCT, comparing amniotomy (N=70) to unrandomized women whose labor progressed spontaneously without intervention (N=70) in nulliparous and multiparous women, there were 3 cases (4%) of intrapartum fever and 1 case (1%) of postpartum fever in the intervention group, as compared with 0 cases of intrapartum or postpartum fever in the control group. There were no cases of postpartum hemorrhage in either group. Pelvic floor trauma was

reported as rates of anal sphincter tear. There were no cases of anal sphincter tear reported in either group.[73]

Neonatal Outcomes after Amniotomy

In one good quality RCT comparing amniotomy shortly after admission (N=340) to control treatment (N=350) in the composite results of nulliparous and multiparous women, there were no cases of neonatal fever in the intervention group (0%) and 1 case (0.3%) in the comparison group (low SOE).[74]

Process-Related Outcomes after Amniotomy

In a good quality RCT, comparing amniotomy (N=70) to control treatment (N=70), maternal satisfaction was reported by a mixed population (multiparous and nulliparous) women on a scale of 1-5. Women randomized to amniotomy reported a similar average maternal satisfaction score (4.7 ± 0.6) as compared to control treatment (5.0 ± 0.1).[73]

Relevant Systematic Reviews/Meta-Analyses for Amniotomy

A single Cochrane good-quality review[79] compared amniotomy alone to control treatment to shorten the duration of labor. The objective of this review was to determine the effectiveness and safety of amniotomy alone for routinely shortening all spontaneous labor. The study included singleton pregnancies regardless of parity or gestation at trial entry in spontaneous labor. This meta-analysis included RCTs comparing amniotomy alone versus intention to preserve the membranes. This review included 15 studies, randomizing a total of 5583 women. One of these 15 studies was also included in our review.[75] The remaining 14 included studies were excluded because of date of publication (prior to January 1, 2005). There was no evidence that amniotomy shortened the duration of labor. There was no reduction in the duration of the first stage of labor (MD -20.43 minutes; 95% CI, -95.93 to 55.06) or increased the risk of cesarean delivery (RR 1.27; 95% CI, 0.99 to 1.63). These findings were also seen in subgroups of nulliparous women only or multiparous women only. There were no statistically significant differences in risk for other maternal or neonatal adverse outcomes.

Strength of Evidence for Amniotomy

Tables 13–15 summarize the SOE for the comparison of amniotomy versus control treatment.

Table 13. Early amniotomy versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	4 RCTs[72-74,77] (1473)	**Improvement with early amniotomy:** All four trials (2 fair quality, 2 good quality) demonstrated a decrease in the duration of labor in women randomized to early amniotomy.	Moderate (Medium risk of bias, Indirect)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	4 RCTs[72-74,77] (1473)	**Inconclusive:** SOE was insufficient given inconsistent and imprecise findings from studies of varying quality.	Insufficient (Medium risk of bias, Indirect, inconsistent, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table 14. Early amniotomy versus control: Strength of evidence in women with unspecified parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	2 RCTs[73,75] (411)	**Inconclusive:** SOE was insufficient given inconsistent findings from 2 studies.	Insufficient (Indirect, inconsistent, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[73,75] (411)	**No difference**: According to two good quality RCTs, there was no difference in the rate of cesarean delivery between women randomized to early amniotomy versus control.	Low (Indirect, imprecise)
Adverse Events			
Maternal Outcomes – Infection	2 RCTs[73,74] (973)	**No difference:** There was no evidence of increased risk of infection associated with early amniotomy versus control.	Moderate (Imprecise)
Maternal Outcomes – Hemorrhage	2 RCTs[73,74] (973)	**No difference:** There was no evidence of increased risk of maternal hemorrhage associated with early amniotomy.	Moderate (Imprecise)
Maternal Outcomes – Trauma to Pelvic Floor	3 RCTs[73,74,77] (683)	**No difference:** There was no evidence of increased risk of trauma to the pelvic floor associated with early amniotomy.	Moderate (Medium risk of bias)
Neonatal Outcomes – Infection	1 RCTs[74] (690)	**No difference:** There was no evidence of increased risk of neonatal infection associated with early amniotomy.	Low (1 study)
Process Related Outcomes – Mode of Delivery (Operative Vaginal Delivery)	3 RCTs[73,75,77] (611)	**No difference:** There was no evidence of increased risk of operative vaginal delivery associated with early amniotomy.	Low (Indirect, imprecise)
Process Related Outcomes – Parental Satisfaction	1 RCT[73] (273)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 small study	Insufficient (Imprecise, 1 small study)

a Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table 15. Early amniotomy versus control: Strength of evidence in multiparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	2 RCTs[73,74] (973)	**Inconclusive:** SOE was insufficient given conflicting evidence from available studies.	Insufficient (Indirect, inconsistent, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[73] (533)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Indirect, imprecise)
Process Related Outcomes – Parental Satisfaction	1 RCT[73] (273)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 small study	Insufficient (Imprecise, 1 small study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Amniotomy plus Oxytocin versus Control Treatment

Labor management with amniotomy is often combined with latent use of oxytocin in labor protocols. Two RCTs examined amniotomy plus oxytocin in this context. One of the two studies reported results for nulliparous and multiparous women combined and for each of the parity subgroups.[73] The other reported results only for nulliparous women.[76]

A good quality RCT[73] examined delivery outcomes in women who were randomized to amniotomy (n=16) as compared to a control group (n=20). In this case, the control group was composed of (unrandomized) women whose labor progressed spontaneously without intervention.

A second RCT[76] compared an active management of labor protocol to control treatment for nulliparous women in spontaneous labor in a low resource setting. Active management was defined as amniotomy within 1 hour of admission, frequent vaginal exams, and routine administration of high dose oxytocin if cervical dilation fell below a rate of 1cm/hour. Control treatment was conventional care at the discretion of the provider. Of note, while patients in the intervention group received oxytocin more frequently than those in the comparison group ($p<0.05$), 47% of patients in the comparison group received oxytocin.

Two relevant good-quality SRs were identified.[30,78] Wei et al.[78] performed a meta-analysis to estimate the effects of amniotomy plus oxytocin for prevention of, or therapy for, delay in labor progress on the cesarean delivery rate and on indicators of maternal and neonatal morbidity. The SR/MA included 14 trials, randomizing a total of 8033 women. Two of these 14 studies are also included in our review.[73,76] The remaining 12 included studies were excluded because of date of publication (prior to January 1, 2005). Given the overlap of our two included studies with the SR, we rated the SOE based on the findings of this SR. The results of SR/MA by Brown et al is summarized in detail in KQ 1.[30]

Results in Nulliparous Women for Amniotomy plus Oxytocin

Duration of Labor and Cesarean Delivery Rates for Amniotomy plus Oxytocin

In two good-quality RCTs of nulliparous women, the first stage and total duration of labor was shortened in women randomized to amniotomy plus oxytocin as compared to control

treatment.[73,76] These findings were also supported by a good-quality SR discussed below and the combined evidence resulted in a high SOE.

Maternal Outcomes after Amniotomy plus Oxytocin

Two good quality RCTs reported maternal outcomes including infection, hemorrhage and pelvic floor trauma and identified no increased risk of maternal adverse outcomes in nulliparous women randomized to amniotomy with oxytocin as compared to control treatment. In nulliparous women, amniotomy and oxytocin does not significantly increase the risk of adverse maternal outcomes as compared with control treatment.

In a good quality RCT, comparing amniotomy (N=16) to unrandomized women whose labor progressed spontaneously without intervention (N=23) in nulliparous women, there were no cases of intrapartum, postpartum fever, antibiotic use, postpartum hemorrhage or anal sphincter tear in either group.[73]

Another good quality RCT compared amniotomy and oxytocin protocol (n=320) to control treatment (n=640) for nulliparous women in spontaneous labor in a low resource setting. There were 26 cases (8.1%) of maternal fever in the intervention group, and 53 cases (8.3%) in the comparison group. There were no cases of postpartum hemorrhage in either group.[76]

Neonatal Outcomes after Amniotomy plus Oxytocin

There was very little information on neonatal adverse outcomes in this subgroup. A good quality RCT, comparing amniotomy and oxytocin protocol (n=320) to control treatment (n=640) for nulliparous women in spontaneous labor in a low resource setting, reported no cases of chorioamnionitis in the intervention group, and 6 cases (0.9%) in the comparison group. The difference was not statistically significant.[76]

Process-Related Outcomes after Amniotomy plus Oxytocin

In a good quality RCT, comparing amniotomy (N=16) to control treatment (N=23), maternal satisfaction was reported by multiparous women on a scale of 1-5. Multiparous women randomized to amniotomy reported a similar average score (4.8 ± 0.5) as compared to control treatment (5.0 ± 0.2; p=0.15).[73]

Results in Multiparous Women for Amniotomy plus Oxytocin

Duration of Labor and Cesarean Delivery Rates for Amniotomy plus Oxytocin

One good-quality RCT[73] examined amniotomy and oxytocin (n= 55) versus control treatment (N=47) in multiparous women. There was a statistically significant decrease in the total duration of labor in the intervention group (279 ± 201 minutes) compared with the control group (376 ± 232 minutes; p=0.03). There was no significant difference in cesarean delivery rates. The cesarean rate in the intervention group was 0.02% and 0.04% in the comparison group.

Maternal Outcomes after Amniotomy plus Oxytocin

One good-quality RCT[73] examined amniotomy and oxytocin (n= 55) versus control treatment (N=47) in multiparous women. There were no cases of intrapartum fever, postpartum fever or antibiotic use in either group. There were 3 cases (6%) of postpartum hemorrhage in the intervention group, there were no cases in the comparison group (p=0.25). There were no cases of anal sphincter tear in either group.

Neonatal Outcomes after Amniotomy plus Oxytocin

No data was available on neonatal adverse outcomes for multiparous women in spontaneous labor randomized to amniotomy and oxytocin as compared with control treatment.

Process-Related Outcomes after Amniotomy plus Oxytocin

In a good quality RCT, comparing amniotomy (N=55) to control treatment (N=47), maternal satisfaction was reported by multiparous women on a scale of 1-5. Multiparous women randomized to amniotomy reported a similar average score (4.9 ± 0.5) as compared to control treatment (5.0 ± 0.0; p=0.14).[73]

Results in Women of Mixed or Unspecified Parity for Amniotomy plus Oxytocin

A single study reported results for amniotomy plus oxytocin versus control treatment in women of mixed parity.[73]

Duration of Labor and Cesarean Delivery Rates for Amniotomy plus Oxytocin

In one good-quality RCT examining women of mixed parity,[73] there was a statistically significant difference in the total duration of labor for women randomized to amniotomy plus oxytocin (n= 71; 312 +/- 245 minute) as compared with control treatment (n= 70; 498+/-306 minutes; p<0.001). There was no difference in cesarean delivery rates between the two treatment groups (1% in both groups).[73]

Maternal Outcomes after Amniotomy plus Oxytocin

One good-quality RCT examined the risks of adverse maternal outcomes in women of mixed parity randomized to amniotomy plus oxytocin (N=71) compared to control (N=70). There was no increased risk of adverse maternal outcomes in either group. There were no cases of intrapartum fever, postpartum fever, or antibiotic use in this subgroup. There were 3 cases of postpartum hemorrhage (4%) in the intervention group as compared to 0 cases in the comparison group. This difference was not statistically significant. There were no cases of anal sphincter injury in either group.[73]

Neonatal Outcomes after Amniotomy plus Oxytocin

No data was available on neonatal adverse outcomes for women of mixed parity in spontaneous labor randomized to amniotomy and oxytocin as compared with control treatment.

Process-Related Outcomes after Amniotomy plus Oxytocin

In a good quality RCT, comparing amniotomy (N=71) to control treatment (N=70), maternal satisfaction was reported by multiparous women on a scale of 1-5. Multiparous women randomized to amniotomy reported a similar average score (4.9 ± 0.5) as compared to control treatment (5.0 ± 0.1; p=.10)[73]

Relevant Systematic Reviews/Meta-Analyses for Amniotomy plus Oxytocin

Wei et al.[78] performed a meta-analysis to estimate the effects of amniotomy plus oxytocin for prevention of, or therapy for, delay in labor progress on the cesarean delivery rate and on indicators of maternal and neonatal morbidity. The SR/MA included 14 trials, randomizing a total of 8033 women. Two of these 14 studies represent the two included studies in our review.[73,76] The remaining 12 included studies were excluded from our report because of date of

publication (prior to January 1, 2005). Studies included unselected pregnant women in spontaneous labor and pregnant women in spontaneous labor with a delay in the first stage of labor. The length of first stage of labor was shortened in the amniotomy plus oxytocin group compared with the expectant management group (mean difference [MD] -1.57 hours; 95% CI, -2.14 to -1.01). Amniotomy plus oxytocin was also associated with a reduction in the total duration of labor (MD -1.28 hours; 95% CI, -1.97 to -0.59). The cesarean delivery rate was reduced in 11 trials looking at prevention of dystocia (11 trials, 7653 women, average RR 0.87; 95% CI, 0.77 to 0.99). In women who were randomized to amniotomy plus oxytocin, the time from admission to giving birth was reduced (MD 1.3 hours; 95% CI, -1.97 to -0.59).

Strength of Evidence for Amniotomy plus Oxytocin

Tables 16–18 summarize the SOE for the comparison of amniotomy plus oxytocin versus control treatment. In general, the SOE was judged as moderate or high based on existing SR/MAs.

Table 16. Amniotomy plus oxytocin versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[73,76] (1,243) 3 SR/MAs[30,78,79] (11,167)	**Improvement with amniotomy plus oxytocin:** Amniotomy plus oxytocin decreased the duration of the first stage of labor.	High
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[73,76] (1,243) 2 SR/MAs[30,79] (8,496)	**No difference:** There was no difference in the duration of second stage of labor between groups.	Moderate (Imprecise)
Process Related Outcomes – Duration of Total Labor	2 RCTs[73,76] (1,243) 3 SR/MAs[30,78,79] (13,312)	**Improvement with amniotomy plus oxytocin:** The duration of labor was shortened in women randomized to amniotomy plus oxytocin as compared to routine care.	High
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[73,76] (1,243) 3 SR/MAs[30,78,79] (16,529)	**No difference:** Based on SR and included RCTs, there was no difference in cesarean delivery rates between amniotomy plus oxytocin compared with control	High

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR/MA=systematic review/meta-analysis

Table 17. Amniotomy plus oxytocin versus control: Strength of evidence in women with unspecified parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[73] (283) 3 SR/MAs[30,78,79] (11,167)	**Improvement with amniotomy plus oxytocin:** Based on SR/MAs and included RCTs, amniotomy plus oxytocin decreased the duration of the first stage of labor.	High

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[73] (283) 2 SR/MAs[30,79] (8,496)	**No difference:** There was no difference in the duration of the second stage of labor in the amniotomy plus oxytocin group as compared with control.	Moderate (Imprecise)
Process Related Outcomes – Duration of Total Labor	1 RCT[73] (283) 3 SR/MAs[30,78,79] (13,312)	**Improvement with amniotomy plus oxytocin:** Based on SR/MAs and included RCTs, amniotomy plus oxytocin decreased the total duration of labor.	High
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[73] (283) 3 SR/MAs[30,78,79] (16,529)	**No difference:** Based on SR/MAs and included RCTs, there was no difference in cesarean delivery rates between amniotomy plus oxytocin compared with control.	High
Adverse Events			
Maternal Outcomes – Infection	3 RCTs[73,74,76] (1,933) 3 SR/MAs[30,78,79] (11,419)	**No difference:** There was no difference in risk of infection between groups.	High
Maternal Outcomes – Hemorrhage	1 RCT[73] (283) 3 SR/MAs[30,78,79] (11,311)	**No difference:** No difference in risk of hemorrhage between groups.	High
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[73] (283)	**No difference:** One RCT examined active management of labor with early amniotomy and oxytocin as compared with routine care, there was no difference in risk of trauma to the pelvic floor between groups.	Low (1 study)
Process Related Outcomes – Mode of Delivery (Operative Vaginal Delivery	2 RCTs[73,76] (1,243) 2 SR/MAs[78,79] (3,096)	**No difference:** There was no difference in risk of operative vaginal delivery between groups.	High
Process Related Outcomes – Parental Preferences	1 RCT[73] (283) 3 SR/MAs[30,78,79] (11,114)	**No difference:** No difference between the two groups in scores of maternal/parental satisfaction.	Moderate (Imprecise, varying metrics)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR/MA=systematic review/meta-analysis

Table 18. Amniotomy plus oxytocin versus control: Strength of evidence in multiparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[73] (283) 3 SR/MAs[30,78,79] (11,167)	**Improvement with amniotomy:** Amniotomy decreased the duration of the first stage of labor compared with control	Moderate (Imprecise)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[73] (283) 2 SR/MAs[30,79] (8,496)	**No difference:** No difference in the duration of second stage of labor between groups.	Moderate (Imprecise)
Process Related Outcomes – Duration of Total Labor	1 RCT [73] (283) 3 SR/MAs[30,78,79] (13,312)	**Improvement with amniotomy plus oxytocin:** Modest decrease in duration of labor in the intervention group as compared with controls.	Moderate (Imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[73] (283) 3 SR/MAs[30,78,79] (16,529)	**No difference:** No difference in the rate of cesarean delivery between groups.	Moderate (Imprecise)

[a]Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR/MA=systematic review/meta-analysis

Key Question 3. Supportive Care

KQ 3 was: What are the benefits and harms of supportive care measures, including ambulation, nutrition, hydration, and emotional support during spontaneous labor?

Description of Included Studies

We identified 44 articles[80-123] representing 42 individual RCTs that examined the benefits and harms of supportive care measures in women during spontaneous labor. Of the 42 included studies, 17 were conducted in the Middle East,[81,83-85,91,94-96,98,101,105,106,111,115-117,122] 11 were conducted in Asia,[80,87,93,97,99,110,113,118,119,121,123] 6 were conducted in the United States,[88,100,102,103,109,114] 3 were conducted in Latin America,[89,104,112] 3 were conducted in UK/Europe,[86,92,107] one was conducted in Australia/NZ,[120] and one was conducted in Canada.[90] All but two studies[87,89] were conducted in a hospital setting. Both of these studies were conducted in birthing centers. Six studies reported government funding,[80,88,99,103,109,112] 17 reported nongovernment, nonindustry funding,[81,84,85,90,91,94,96,98,100,111,113,115-118,121,123] and one reported a mixture of funding from government and non-government sources.[86] Eighteen studies were unclear or did not report the funding source.[83,87,89,92,93,95,97,101,102,104-107,110,114,119,120,122] Finally, of the 42 included studies, 17 were rated as good quality,[89,90,93,97,99,100,102-104,106,107,109,111-113,120,123] 18 as fair quality,[80,83,86-88,91,92,94,95,98,101,105,114-118,122] and 7 as poor quality.[81,84,85,96,110,119,121]

In addition to the above studies, eight SRs that addressed the benefits and harms of supportive care measures are also discussed below.[29,31,33,40,43,45,47,49] All of these SRs were rated as good quality.

Key Points for Supportive Care

- Supportive care measures during labor encompass a wide variety of interventions and within individual categories of interventions, there is considerable heterogeneity in the nature and timing of the interventions.
- Although supportive care therapies are often seen as benefiting parental satisfaction with the birthing process, these outcomes were only assessed in 5 of our included RCTs with

sparse evidence. An existing SR of 11 studies however did find that women receiving continuous emotional support were less likely to rate their birth experience negatively (moderate SOE).

- Two studies addressing continuous emotional support included in the present review did not show a benefit in reducing 1st or 2nd stage labor duration, although prior SR/MAs of 12 studies (including these two studies) indicated a benefit for total labor duration (moderate SOE).
- Emotional support interventions reduced cesarean deliveries (low SOE for doula support, moderate SOE for continuous emotional support) and instrumental deliveries (moderate SOE).
- There was no difference in rates of cesarean deliveries for women receiving perienal compresses or massage (low SOE), but severe perineal trauma was reduced in nulliparous women (low SOE).
- There was no difference in duration of labor in women using water birth (low SOE)
- Women undergoing acupuncture/acupoint nerve stimulator did not experience differences in labor duration or rates of maternal hemorrhage (low SOE for both outcomes).
- Ambulation was associated with reduced duration of duration of labor (low SOE).
- No differences were found in duration of labor (low SOE) or cesarean delivery rates (moderate SOE) for women using differing positioning interventions. Women in kneeling position were more likely than women in sitting position to have reduced trauma to the pelvic floor (low SOE).
- Administration of intravenous fluids compared with oral intake alone demonstrated a reduction in the duration of labor (low SOE), while not increasing cesarean delivery rates (moderate SOE), maternal hemorrhage (low SOE), or operative vaginal delivery rates (moderate SOE).

Detailed Synthesis for Supportive Care

The supportive care interventions as compared with control treatment were:

1. Continuous emotional support
2. Perineal compresses or massage
3. Massage during labor
4. Water birth
5. Acupressure
6. Acupuncture
7. Aromatherapy
8. *Anetheum graveolens* seeds
9. Ambulation and positioning strategies
10. Specific nutritional or oral or parenteral hydration recommendations or limitations

Below we detail each of these comparisons in terms of the included studies, outcomes assessed, and strength of evidence. Within each comparison we discuss findings in nulliparous women, in multiparous women, and then in women of mixed or unspecified parity.

1. Continuous Emotional Support versus Control Treatment

Results for this intervention were reported for nulliparous women in three studies[103,112,123] and for a mixed population of women in one study (two articles).[81,82] Two relevant good-quality SR/MAs were identified.[47,49]

Results in Nulliparous Women

Three studies[103,112,123] examined the effects of continuous emotional support during labor provided by either a doula[103] or a relative or companion of the patient's choosing.[112,123] All three studies were good quality.[103,112,123]

Duration of Labor and Cesarean Delivery Rates for Continuous Emotional Support

No significant difference in duration of labor was reported in the two primary studies reporting on this outcome.[112,123] The duration of first-stage labor was nonsignificantly shorter in the companion arm [(3.4 vs. 3.8 hours, p=0.123)[112] and (4.48 vs. 5.02 hours, p=0.09)[123]] The duration of second-stage labor was non-significantly longer in the companion arm in both studies [(18 vs. 16.2 minutes, p=0.368)[112]; (58 vs. 50.1 minutes, p=0.26)[123]]. These findings were also included in the SR discussed below and based on that larger set of studies we found a moderate strength of evidence that there was an overall reduction in duration of labor for women receiving emotional support.

Cesarean deliveries were reported significantly less often in the doula arm in one study (13.4% vs. 25.0%, p=0.002),[103] whereas a similar proportion of cesarean deliveries was reported in both treatment arms in another study (10.5% in the continuous support arm vs. 11.2% in the control arm, RR 0.93, 95% CI 0.43 to 2.02).[112] Based on these findings in combination with the SR evidence discussed below we rated the SOE as low for a reduction in cesarean deliveries with doula support.

Neonatal Outcomes for Continuous Emotional Support

No significant difference was reported for altered fetal heart rate in one study (RR 1.18, 95% CI 0.84 to 1.66) (low SOE).[112]

Results in Women of Mixed or Unspecified Parity

Duration of Labor and Cesarean Delivery Rates for Continuous Emotional Support

One poor-quality study reported in two separate articles,[81,82] evaluated duration of labor in a mixed population of 150 nulliparous and multiparous women. The duration of labor in the group receiving continuous emotional support from a doula was significantly shorter than the control group for first-stage labor (157 vs. 281 minutes, p<0.001) and second-stage labor (58.9 vs. 128.4 minutes, p<0.001).[81] Given the small size of the single study and the poor quality, the evidence was rated as insufficient for all outcomes assessed.

Relevant Systematic Reviews/Meta-Analyses for Continuous Emotional Support

We identified two good-quality SR/MAs that addressed either doula support[47] or continuous emotional support[49] during labor. Doula support compared with standard care was associated

with a significantly reduced risk of cesarean delivery (OR 0.68, 95% CI 0.47 to 0.99) based on 2008 women across 5 studies (low SOE) and reduced risk of instrumental vaginal delivery (OR 0.54, 95% CI 0.35 to 0.92) based on 1587 women across 4 studies (moderate SOE).[47] One study included in the present review was included in this SR.[103]

Continuous emotional support was associated with a shorter total duration of labor (mean difference -0.58 hours, 95% CI -0.85 to -0.31) based on 5366 women across 12 studies (moderate SOE).[49] It also was associated with a lower risk of cesarean delivery (RR 0.78, 95% CI 0.67 to 0.91) based on 15,175 women across 22 studies (moderate SOE), a lower risk on instrumental vaginal delivery (RR 0.90, 95% CI 0.85 to 0.96) based on 14,118 women across 19 studies (moderate SOE), and a higher risk of spontaneous vaginal delivery (RR 1.08 95% CI 1.04 to 1.12) based on 14,119 women across 19 studies.[49] Women receiving continuous emotional support were also less likely to rate their birth experience negatively (RR 0.69, 95% CI 0.59 to 0.79), based on 11,133 women across 11 studies (moderate SOE).[49] No significant differences were observed for trauma to the pelvic floor or neonatal admission to special care nursery.[49] Three of the studies included in the present review were included in the SR/MAs of continuous emotional support.[103,112,123]

Strength of Evidence for Continuous Emotional Support

Tables 19 and 20 summarize the SOE for the above outcomes in nulliparous and mixed parity women.

Table 19. Continuous emotional support versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[112,123] (326)	**No difference:** Good-quality studies of nulliparous women found that continuous emotional support did not reduce duration of 1st stage labor.	Moderate (Indirect)
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[112,123] (326)	**No difference:** Good-quality studies of nulliparous women found that continuous emotional support did not reduce duration of 2nd stage labor.	Moderate (Indirect)
Process Related Outcomes – Duration of Total Labor	1 SR[49] (5,366)	**Improvement with continuous emotional support:** Systematic review of 12 studies found shorter total duration of labor (mean difference -0.58 hr, 95% CI -0.85 to -0.31).	Moderate (Indirect)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[103,112] (599) 2 SRs[47,49] (17,583)	**Improvement with Doula support:** Doula support reduced cesarean deliveries as compared to control therapy. Existing SR of 5 studies demonstrated reduced risk of cesarean delivery with doula support. The inconsistency amongst our 2 included RCTs lowered the SOE to low. **Improvement with continuous emotional support:** Continuous emotional support lowered risk of cesarean delivery (RR 0.78, 95% CI 0.67 to 0.91) based on SR of 22 studies.	Low – Doula (Indirect, inconsistent) Moderate – Continuous Emotional Support (Indirect)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Mode of Delivery (Instrumental Delivery)	2 SRs[47,49] (15,705)	**Improvement with Doula support:** Doula support reduced risk of instrumental vaginal delivery (OR 0.54, 95% CI 0.35 to 0.92). **Improvement with continuous emotional support:** Continuous emotional support lowered risk of instrumental vaginal delivery (RR 0.90, 95% CI 0.85 to 0.96) based on SR of 19 studies.	Moderate (Indirect)
Adverse Events			
Process Related Outcomes – Abnormal Fetal Heat Tracing	1 RCTs[112] (212)	**No difference:** Supportive care was not associated with significant differences in fetal heart tracings.	Low (Indirect, imprecise, 1 study)
Process Related Outcomes – Parental Preferences	1 SR[49] (11,113)	**Improvement with continuous emotional support:** SR of 11 studies found women receiving continuous emotional support less likely to rate their birth experience negatively (RR 0.69, 95% CI 0.59 to 0.79).	Moderate

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; hr=hours; RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence; SR=systematic review

Table 20. Continuous emotional support versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[81] (150)	**Inconclusive:** SOE was insufficient given 1 small study with high risk of bias.	Insufficient (High risk of bias, Indirect, imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[81] (150)	**Inconclusive:** SOE was insufficient given 1 small study with high risk of bias.	Insufficient (High risk of bias, Indirect, imprecise)
Process Related Outcomes – Duration of Total Labor	1 RCT[81] (150)	**Inconclusive:** SOE was insufficient given 1 small study with high risk of bias.	Insufficient (High risk of bias, Indirect, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence

2. Perineal Compresses or Massage versus Control Treatment

Results for this intervention were reported for nulliparous women in two studies (one good quality)[120] and one fair quality[116]) and for a mixed population of women in one good-quality study.[109] No relevant SR/MAs were identified.

Results in Nulliparous Women

Two studies, assessed the effects of perineal compresses or massage on labor outcomes, including duration of labor, cesarean delivery rate, and incidence of perineal trauma. The interventions were warm compresses applied to the perineum during second-stage labor[120] or cold compresses applied to the body during first-stage labor and to the perineum during second-stage labor.[116]

Duration of Labor and Cesarean Delivery Rates for Perineal Compresses or Massage

Warm compresses or perineal massage showed no statistically significant difference in duration of second-stage labor (82.09 vs. 86.64 minutes, p=0.35),[120] whereas a statistically significant shortening of both first-stage (190.44 vs. 273.91 minutes, p<0.001) and second-stage (32.12 vs. 41.15 minutes) labor was reported with cold compresses.[116] Given the inconsistent findings for second-stage labor and to small number of patients in the fair-quality study for first-stage labor, both these outcomes were rates as insufficient SOE. The proportion of cesarean deliveries was not significantly different for women who had warm compresses applied to the perineum (12/360 in the intervention group vs. 8/357 in the control group, p=0.64) (low SOE).

Maternal Outcomes for Perineal Compresses or Massage

Severe perineal trauma (third- and fourth-degree perineal laceration) was reported in one study, with a significantly lower incidence in the intervention group (4.2% vs. 8.7%, OR 2.16, 95% CI 1.15 to 4.10).[120] A significantly lower rate of urinary incontinence at 3 months in the intervention care group was also reported (9.7% vs. 22.4, p=0.0001).[120]. Strength of evidence was rated as low for both outcomes.

Results in Women of Mixed or Unspecified Parity

One good-quality study compared compresses applied to the perineum versus perineal massage versus control treatment in a population comprised on nulliparous and multiparous women.[109]

Duration of Labor and Cesarean Delivery Rates for Perineal Compresses or Massage

The duration of second-stage labor was not statistically significantly different between the intervention groups (41 minutes for warm compresses, 33 minutes for perineal massage, and 36 minutes for control treatment).[109] Spontaneous vaginal delivery occurred in 96.0% of the warm compress group, 99.3% of the perineal massage group, and 98.5% of the control group.[109] The SOE was rated as low for both outcomes.

Maternal Outcomes for Perineal Compresses or Massage

Third- or fourth-degree perineal trauma was reported for 0.7% of the warm compress group, 1.3% of the perineal massage group, and 1.5% of the control group (p value not reported) low SOE).[109]

Strength of Evidence for Perineal Compresses or Massage

Tables 21 and 22 summarize the SOE for the above studies. In general the SOE was rated as low given evidence from only one study.

Table 21. Perineal compresses or massage versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[116] (64)	**Inconclusive:** SOE was rated as insufficient given findings from 1 small study with medium risk of bias.	Insufficient (Medium risk of bias, indirect, 1 small study)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[116,120] (781)	**Inconclusive:** SOE was rated as insufficient given inconsistent findings from 2 studies with medium risk of bias.	Insufficient (Medium risk of bias, Inconsistent, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[120] (717)	**No difference:** No significant differences in the proportion of cesarean deliveries was reported for the massage/compress group.	Low (Indirect, 1 study)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[120] (717)	**Improvement with massage/compress:** Severe perineal trauma (third- and fourth-degree perineal laceration) was lower incidence for the massage/compress group (OR 2.16, 95% CI 1.15 to 4.10).	Low (1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; OR=odds ratio; RCT=randomized controlled trial; SOE=strength of evidence

Table 22. Perineal compresses or massage versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[109] (1,211)	**No difference:** Duration of 2nd stage labor was not statistically significantly different between the intervention and usual care groups.	Low (Indirect, 1 study)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[109] (1,211)	**No difference:** No significant differences in the proportion of cesarean deliveries was reported for the massage/compress group.	Low (Indirect, 1 study)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[109] (1,211)	**No difference:** No significant differences in perineal trauma were reported between the intervention and control groups.	Low (1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

3. Massage During Labor versus Control Treatment

Results for massage during labor versus control treatment were reported for nulliparous women in three studies.[89,90,96] No relevant SR/MAs were identified.

Results in Nulliparous Women

Three studies, two good quality[89,90] and one poor quality,[96] evaluated the effects of massage during labor. The duration and timing of the intervention varied between studies ranging from 30 minutes of massage[89] up to 5 hours of massage.[90]

Duration of Labor and Cesarean Delivery Rates for Massage During Labor

Duration of labor (first- or second-stage or total duration) was not significantly different between the massage and control groups in the two good-quality studies (Table 23).[89,90] The poor-quality study reported that the active phase of labor was 3.1 hours shorter in the massage group ($p<0.001$).[96] Based on these findings the SOE was rated as insufficient for the duration of 1st stage labor and for 2nd stage but low for the total duration of labor.

Additionally, the proportion of cesarean deliveries was not significantly different between the massage groups and control groups in the two studies reporting this outcome (low SOE).

Table 23. Effects of massage during labor versus control treatment

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value
Silva Gallo, 2013[89] Good	Massage (30 min) adjunct to usual care N=23	Usual care N=23	Total duration 6.8 hr (1.6)	Total duration 5.7 hr (1.5)	Mean difference (95% CI) 1.1 (0.2 to 2.0)	6/23	4/23	RR 1.5, 95% CI 0.5 to 4.6
Janssen, 2012[90] Good	Massage (up to 5 hr) adjunct to usual care N=37	Usual care N=40	1st stage 897.4 min (507.4) 2nd stage 136.0 min (89.6)	1st stage 788.6 min (336.8) 2nd stage 125.0 min (81.7)	0.28 0.36	9/37	7/40	0.71
Mortazavi, 2012[96] Poor	Massage (30 min x 3) adjunct to usual care N=40	Usual care N=40	Active phase 2.6 hr (0.95)	Active phase 5.7 hr (1.89)	<0.001	–	–	–

Abbreviations: Com=comparator; hr=hours; Int=intervention; min=minutes; RR=relative risk

Strength of Evidence for Massage During Labor

Table 24 summarizes the SOE for the effects of massage during labor.

Table 24. Massage during labor versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[90,96] (197)	**Inconclusive:** SOE was insufficient given inconsistent and imprecise findings from 2 studies.	Insufficient (Medium risk of bias, indirect, Inconsistent, imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[90] (77)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 small study.	Insufficient (Indirect, Imprecise, 1 small study)
Process Related Outcomes – Duration of Total Labor	2 RCTs[89,90] (123)	**No difference:** Total duration of labor was not significantly different in the massage group compared to usual care.	Low (Indirect, Imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[89,90] (123)	**No difference:** The proportion of cesarean deliveries was not significantly different between the massage group and control group.	Low (Indirect, Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

4. Water Birth versus Control Treatment

Results for this intervention were reported for women of mixed parity in one study.[101] One relevant good-quality SR/meta-analysis was also identified.[43]

Results in Women of Mixed or Unspecified Parity

One RCT of fair quality assessed labor outcomes among 106 women giving birth in a warm water bath compared with conventional deliveries.[101] First-stage active labor was significantly shorter in the water birth group (114.4 vs. 186 minutes, p=0.004), whereas no difference was observed in duration of second-stage labor (20.9 vs. 20.6 minutes, p=0.9). All water births were vaginal deliveries compared with 79.2% in the conventional group.

Relevant Systematic Reviews/Meta-Analyses for Water Birth

We identified one good-quality SR/meta-analysis that addressed the effects of immersion in water on labor outcomes.[43] Analyses that were restricted to women in spontaneous labor included 1 to 3 studies, with 60 to 286 women included in different analyses. No statistically significant differences were observed in length of first- or second-stage labor, cesarean deliveries, hemorrhage, perineal trauma, neonatal ICU admission, or neonatal sepsis. Based on one study within that meta analysis, women who gave birth in water immersion were less likely to report being dissatisfied with their birth experience (RR 0.24, 95% CI 0.07 to 0.80). The one study included in the present review was also included in the SR/meta-analysis.[101]

Given the findings of this sole fair-quality RCT and the combined evidence from the SR we rated the SOE for total duration of labor as low for no difference between water birth and control and insufficient for the outcome of cesarean delivery.

Strength of Evidence for Water Birth

Table 25 summarizes the SOE for water birth compared to control therapy.

Table 25. Water birth versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[101] (106) 1 SR[43] (286)	**No difference:** No difference in duration of 2nd stage labor was reported between the water birth and usual care groups. SOE was increased to low given findings from SR which also demonstrated no difference between water birth versus control.	Low (Medium risk of bias, indirect, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[101] (106) 1 SR[43] (180)	**Inconclusive:** SOE was rated as insufficient given inconsistent findings between included studies with potential risk of bias.	Insufficient (Medium risk of bias, Indirect, inconsistent, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

5. Acupressure versus Control Treatment

Results for this intervention were reported for nulliparous women in two studies[111,122] and for women of unspecified parity in two studies.[81,95] One study was judged to be good quality,[111] two fair quality,[95,122] and one poor quality.[81] No relevant SR/MAs were identified.

Results in Nulliparous Women

Duration of Labor and Cesarean Delivery Rates for Acupressure

One good-quality[111] and one fair-quality[122] study assessed duration of labor in nulliparous women. Each measure of duration of labor was significantly shorter for the acupressure group compared with the control group: active phase (4.2 vs. 7.4 hours, p=0.0001),[111] total first-stage (6.02 vs. 9.45 hours, p=0.002),[122] and second-stage (23.42 vs. 34.89 minutes, p=0.04).[122] Given the small size of the studies, the imprecision in the findings, and the potential risk of bias the strength of evidence for all duration of labor outcomes was rated as insufficient. One good-quality study reported a smaller proportion of cesarean deliveries in the acupressure group compared with the control group (6/60 vs. 25/60, p=0.0001) (insufficient SOE).[111]

Results in Women of Mixed or Unspecified Parity

Duration of Labor and Cesarean Delivery Rates for Acupressure

One fair-quality[95] and one poor-quality[81] study assessed duration of labor in mixed populations of nulliparous and multiparous women. Each study reported a statistically significantly shorter duration of first-stage labor (161.7 vs. 281.0 minutes, p<0.0001[81] and 146.4 vs. 185.4 minutes, p<0.001[95] and second-stage labor (56.1 vs. 128.4 minutes, p<0.0001[81] and 20.51 vs. 28.5 min, p=0.038.[95] The lower quality of these included studies and the imprecision of the findings resulted in a insufficient strength of evidence rating for these outcomes.

In the fair-quality study, women in the acupressure group were significantly more satisfied with the birth process than those in the control group (5.76 [0.63] vs. 5.36 [1.08], respectively) (insufficient SOE).[95]

Strength of Evidence for Acupressure

Tables 26 and 27 summarize the SOE for available outcomes within this comparison. Although findings were consistent between studies, the SOE was rated as insufficient for all outcomes given the small number of patients, the potential risk of bias, and the imprecision of the findings.

Table 26. Acupressure versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[122] (100)	**Inconclusive:** SOE was insufficient given potential risk of bias, imprecise findings, and only one study	Insufficient (Medium risk of bias, indirect, imprecise, 1 study)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[122] (100)	**Inconclusive:** SOE was insufficient given potential risk of bias, imprecise findings, and only one study.	Insufficient (Medium risk of bias, indirect, Imprecise, 1 study)
Process Related Outcomes – Duration of Total Labor	2 RCTs[111,122] (220)	**Inconclusive:** SOE was insufficient given potential risk of bias, imprecise findings, and small study size	Insufficient (Medium risk of bias, indirect, Imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCTs[111] (120)	**Inconclusive:** SOE was insufficient given imprecise findings from only one study	Insufficient (Indirect, Imprecise, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table 27. Acupressure versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[81,95] (250)	**Inconclusive:** SOE was insufficient given potential risk of bias, imprecise findings, and small studies	Insufficient (High risk of bias, indirect, Imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[81,95] (250)	**Inconclusive:** SOE was insufficient given potential risk of bias, imprecise findings, and small studies	Insufficient (High risk of bias, indirect, Imprecise)
Process Related Outcomes – Duration of Total Labor	2 RCTs[81,95] (250)	**Inconclusive:** SOE was insufficient given potential risk of bias, imprecise findings, and small studies	Insufficient (High risk of bias, indirect, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

6. Acupuncture versus Control Treatment

Five studies reported on the effects of acupuncture[83,84,86,99] or acupoint nerve stimulator[80] on labor outcomes. Results were reported for nulliparous women in two studies[83,86] and for women of mixed parity in three studies.[80,84,99] One study was good quality,[99] three were fair quality,[80,83,86] and one was poor quality.[84] Comparisons included both sham acupuncture[83,99] and control treatment of either no analgesia or available standard of care.[80,84,86,99] One study compared both acupuncture and electroacupuncture with control treatment[86] and another compared electroacupuncture to sham acupuncture and control treatment.[99] One relevant good-quality SR/meta-analysis was identified.[40]

Results in Nulliparous Women

Duration of Labor and Cesarean Delivery Rates for Acupuncture

Results were not consistent across studies or within one study in regard to the duration of labor (Table 24). The acupuncture group had a significantly shorter duration of first-stage labor when compared with sham acupuncture (130 vs. 250 minutes, p=0.001) but no difference in second-stage labor (36 vs. 35 minutes, p=0.739) in one study.[83] The other study found no significant difference in total duration of labor between the acupuncture and control group (619 vs. 615 minutes, HR 1.03, 95% 0.75 to 1.41), but a significantly shorter duration of labor in the electroacupuncture group (500 vs. 615 minutes, HR 1.44, 95% 1.06 to 1.97).[86] Given the inconsistency of findings and variability in interventions, the SOE was rated as insufficient for the duration of first stage and total duration of labor. The consistency of findings for second stage resulted in a low SOE rating for no difference.

The proportion of cesarean deliveries was smaller, but not significantly different for the acupuncture (8.4%, OR 0.64, 95% CI 0.23 to 1.79) or electroacupuncture (5.7%, OR 0.41, 95% CI 0.14 to 1.26) groups compared with the control group (13.3%).[86] In the other study, the cesarean delivery rates were lowered in the intervention groups as compared to control therapy.[80] Given the inconsistency in findings the SOE was rated as insufficient.

Maternal Outcomes for Acupuncture

Perineal trauma (third or fourth degree laceration) was not significantly different in the acupuncture group (5.3%, OR 1.19, 95% CI 0.28 to 5.16) or electroacupuncture group (4.9%, OR 0.92, 95% CI 0.21 to 3.92) compared with the control group (5.6%) (insufficient SOE).[86]

Results in Women of Mixed or Unspecified Parity

Duration of Labor and Cesarean Delivery Rates for Acupuncture

One study reported a significantly shorter duration of active-phase labor[84] in the acupuncture group, whereas the other two studies found no significant differences in duration of the first-stage, the second-stage, or total duration of labor when comparing the acupuncture group with the control group or with a sham acupuncture group (insufficient SOE for first stage labor, low SOE for no difference in second stage labor duration).[80,99] In one fair-quality study, acupuncture was associated with a significant reduction in cesarean deliveries (1/30 vs. 8/30, $p<0.05$) (insufficient SOE).[80] Table 28 shows results for these studies.

Maternal Outcomes for Acupuncture

Postpartum hemorrhage was not significantly different between the acupuncture and control groups, with one study reporting severe hemorrhage in 8.0% of the control group and 4.0% of the acupuncture group ($p=0.537$),[84] and another study stating no significant differences in postpartum hemorrhage without reporting specific data.[99]

Table 28. Effects of acupuncture versus control treatment

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value
Allameh, 2015[84] Poor	Acupuncture adjunct to usual care N=27	Usual care N=28	Active phase 175.8 min	Active phase 243.77 min	Mean difference <0.001	2/27	3/28	0.67
Ma, 2011[99] Good	Electro-acupuncture adjunct to usual care N=92	Usual care N=100	1st stage latent 219.60 min (130.19)	1st stage latent 244.20 min (164.76)	0.25	–	–	–
	Sham acupuncture adjunct to usual care N=94	Usual care N=100	1st stage latent 246.60 min (161.54)	1st stage latent 244.20 min (164.76)	0.92	–	–	–
	Electro-acupuncture adjunct to usual care N=92	Usual care N=100	1st stage active 186.05 min (99.66)	1st stage active 161.03 min (87.23)	0.06	–	–	–
	Sham acupuncture adjunct to usual care N=94	Usual care N=100	1st stage active 196.76 min (100.91)	1st stage active 161.03 min (87.23)	0.009	–	–	–

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value
	Electro-acupuncture adjunct to usual care N=92	Usual care N=100	2nd stage 30.65 min (19.40)	2nd stage 31.92 min (19.99)	0.66	–	–	–
	Sham acupuncture adjunct to usual care N=94	Usual care N=100	2nd stage 30.02 min (19.39)	2nd stage 31.92 min (19.99)	0.50	–	–	–
	Electro-acupuncture adjunct to usual care N=116	Usual care N=100	Total duration 443.44 min (176.88)	Total duration 444.21 min (193.34)	0.97	–	–	–
	Sham acupuncture adjunct to usual care N=117	Usual care N=100	Total duration 480.85 min (206.80)	Total duration 444.21 min (193.34)	0.16	–	–	–
Liu, 2015[80] Fair	Acupuncture N=30	No analgesic intervention/expectant management N=30	1st stage 430.1 min (119.8)	1st stage 439.6 min (200.3)	0.82	1/30	8/30	0.011
	Acupuncture N=30	No analgesic intervention/expectant management N=30	2nd stage 43.3 min (17.5)	2nd stage 46.3 min (20.6)	0.54	–	–	–

Abbreviations: Com=comparator; Int=intervention; min=minute; NS=not significant

Relevant Systematic Reviews/Meta-Analyses for Acupuncture

We identified one good-quality SR/MA that examined the effects of acupuncture on labor outcomes.[40] Analyses that were restricted to women in spontaneous labor included 1 to 3 studies, with 128 to 448 women in the various analyses of mode of delivery. No statistically significant differences were observed in the proportion of cesarean deliveries, assisted vaginal births, or spontaneous vaginal births.

Strength of Evidence for Acupuncture

Tables 29 and 30 summarize the SOE for acupuncture/acupoint nerve stimulator versus control therapy. In general, the SOE was rated as insufficient given inconsistent findings from studies with variability in interventions.

Table 29. Acupuncture/acupoint nerve stimulator versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	4 RCTs[80,83,84,99] (524)	**Inconclusive:** SOE was insufficient given inconsistency in findings, variability in interventions, and potential risk of bias within the studies.	Insufficient (High risk of bias, indirect, inconsistent, imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[80,99] (350)	**No difference:** No significant difference in 2nd stage labor between the acupuncture and control groups was reported.	Low (Medium risk of bias, indirect, Imprecise)
Process Related Outcomes – Duration of Total Labor	3 RCTs[83,86,99] (602)	**Inconclusive:** SOE was insufficient given inconsistency in findings, variability in interventions, and potential risk of bias within the studies.	Insufficient (Medium risk of bias, indirect, inconsistent, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[80,86] (373)	**Inconclusive:** SOE was insufficient given inconsistency in findings, variability in interventions, and potential risk of bias within the studies.	Insufficient (Medium risk of bias, indirect, inconsistent, imprecise)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[86] (253)	**Inconclusive:** SOE was rated as insufficient given findings from 1 study with medium risk of bias.	Insufficient (Medium risk of bias, Imprecise, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table 30. Acupuncture/acupoint nerve stimulator versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	4 RCTs[80,83,84,99] (524)	**Inconclusive:** Results were inconsistent as to the effects of manual or electroacupuncture on duration of 1st stage labor, with a shorter duration reported in some but not all studies resulting in insufficient SOE.	Insufficient (Medium risk of bias, indirect, inconsistent, imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[80,99] (350)	**No difference:** No significant difference in 2nd stage labor between the acupuncture and control groups was reported.	Low (Medium risk of bias, indirect, imprecise)
Process Related Outcomes – Duration of Total Labor	3 RCTs[83,86,99] (602)	**Inconclusive:** Results were inconsistent as to the effects of manual or electroacupuncture on total duration labor, with a shorter duration reported in only 1 study. SOE was rated as insufficient.	Insufficient (Medium risk of bias, indirect, Inconsistent, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[80,86] (373)	**Inconclusive:** SOE was rated as insufficient given findings from 1 study with medium risk of bias.	Insufficient (Medium risk of bias, indirect, imprecise)
Adverse Events			
Maternal Outcomes – Hemorrhage	1 RCT[86] (253)	**No difference:** No significant difference in hemorrhage was reported for the intervention group compared to the control.	Low (High risk of bias, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

7. Aromatherapy versus Control Treatment

Aromatherapy was compared to control therapy for nulliparous women in two studies, one fair quality[117] and one poor quality.[85] No relevant SR/MAs were identified.

Results in Nulliparous Women

Duration of Labor and Cesarean Delivery Rates for Aromatherapy

In one study, lavender aromatherapy was not associated with a significantly shorter first-stage labor (3.6 vs. 3.9 hours).[117] In the second study, salvia aromatherapy was associated with a significantly shorter duration of first-stage labor (460.3 vs. 509.3 minutes, p=0.001), whereas no significant difference was found for jasmine aromatherapy (493.6 minutes, p=0.4 vs. control treatment). Similar findings were reported for second-stage labor, with durations of 44.3 minutes for salvia aromatherapy, 46 minutes for jasmine aromatherapy, and 49.83 minutes for control treatment (p=0.003 for salvia vs. control treatment).

No significant difference in the proportion of cesarean deliveries was reported in one study.[85] The proportion of cesarean deliveries was 6/52 for the salvia aromatherapy group, 4/52 for the jasmine aromatherapy group and 7/52 for the control group.

In the fair-quality study, women were more "content" (51.2%) compared with those in the control group (23.8%) (p<0.001) (insufficient SOE).[117]

Strength of Evidence for Aromatherapy

Table 31 summarizes the SOE for outcomes comparing aromatherapy and control treatment. Given the potential risk of bias, small study size, and inconsistent findings, the SOE was rated as insufficient for all outcomes.

Table 31. Aromatherapy versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[85,117] (299)	**Inconclusive:** SOE was rated as insufficient given inconsistent findings among studies with potential risk of bias.	Insufficient (High risk of bias, indirect, inconsistent, imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[85] (139)	**Inconclusive:** SOE was rated as insufficient given inconsistent findings among types of aromatherapy from 1 study with high potential risk of bias.	Insufficient (High risk of bias, indirect, imprecise, 1 study)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[85] (156)	**Inconclusive:** SOE was rated as insufficient findings from 1 study with high potential risk of bias.	Insufficient (High risk of bias, indirect, Imprecise, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

8. *Anetheum Graveolens* (Dill) Seeds versus Control Treatment

Results for this intervention were reported for nulliparous and multiparous women in one study.[115] No relevant SR/MAs were identified.

Results in Nulliparous Women

One fair-quality RCT evaluated the effect of consumption of a boiled extract of *Anetheum graveolens L.* (dill) seeds at the start of active-phase labor on duration of labor.[115] Statistically significantly shorter durations of labor were reported for the intervention group for both first-stage (192.01 vs. 397.71 minutes, p=0.001) and second-stage labor (23.10 vs. 39 minutes, p=0.001). Given that the findings are from one small fair-quality study the SOE was rated as insufficient.

Results in Multiparous Women

The same fair-quality study[115] reported outcomes for multiparous women. Duration of first-stage labor was statistically significantly shorter in the intervention group (145 vs. 279.69 minutes, p=0.001), whereas differences for second-stage labor were not significant (12.50 vs. 16.56 minutes, p=0.12). Again given that the findings are from one small fair-quality study the SOE was rated as insufficient.

Strength of Evidence for *Anetheum Graveolens* (Dill) Seeds

Placeholder Tables 32 and 33 summarize the SOE for dill seeds versus control treatment.

Table 32. Anetheum graveolens seeds versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[115] (103)	**Inconclusive:** SOE was rated as insufficient given imprecise findings from 1 small study with potential risk of bias.	Insufficient (Medium risk of bias, indirect, imprecise, 1 study)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[115] (103)	**Inconclusive:** SOE was rated as insufficient given imprecise findings from 1 small study with potential risk of bias.	Insufficient (Medium risk of bias, indirect, imprecise, 1 study)

Table 33. Anetheum graveolens seeds versus control: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)**
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[115] (103)	**Inconclusive:** SOE was rated as insufficient given imprecise findings from 1 small study with potential risk of bias.	Insufficient (Medium risk of bias, indirect, imprecise, 1 study)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[115] (103)	**Inconclusive:** SOE was rated as insufficient given imprecise findings from 1 small study with potential risk of bias.	Insufficient (Medium risk of bias, indirect, imprecise, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

9. Ambulation and Positioning Strategies versus Control Treatment

Twelve studies examined the effects of ambulation and positioning strategies during labor on labor outcomes.[87,92,98,104,105,107,110,113,114,118,119,121] Three of these studies were rated as good-quality[104,107,113] and six studies were rated as fair quality.[87,92,98,105,114,118] Three studies were

judged to be of poor quality[110,119,121] due to unclear and inconsistent reporting, discrepant participant numbers, and poor control group/usual care definitions.

Results were reported for nulliparous women in 10 studies.[87,92,98,104,107,110,113,118,119,121] Table 34 shows results for these studies.

Results were reported for a mixed population of women in two studies.[105,114] Two relevant good-quality SR/MAs were identified.[29,45]

Results in Nulliparous Women

One good-quality study[113] and one poor-quality study[110] examined the effects of ambulation (moving, swaying, rocking, etc.) compared with being confined to bed. Eight studies examined positioning using various methods: angle of the head of the birthing bed,[87] birth seat,[92] birth ball,[98] peanut ball,[119] upright position,[104] kneeling position,[107] and the Prince of Songkla University (PSU) birthing bed.[118,121]

Duration of Labor and Cesarean Delivery Rates for Ambulation and Positioning Strategies

Ambulation during first-stage labor was associated with significant reduction in labor duration compared with confinement to bed in two studies ($p<.05$[113]; $p<.001$[110]) (low SOE). Studies investigating upright laboring positions demonstrated heterogeneity in both interventions and comparators. None of the three studies reporting labor duration data that examined an upright position such as sitting or kneeling during first- or second-stage labor identified statistically significant differences when compared with lying supine[104,119] or sitting with the head of the bed raised 60 degrees.[107] However, one study comparing a semi-sitting (head of bed at 45 degrees) position to a supine position found significant differences in duration of second-stage labor ($p<.05$).[87] Using a birth seat, which may help maintain an upright position, was found to significantly reduce duration of second-stage labor ($p<.001$) compared with all other positions in one study.[92] By comparison, another study compared reclining in bed with use of a birth ball, which may also help maintain an upright position, and did not find significant differences in duration of active-phase labor.[98] The strength of evidence was rated as low for duration of the first stage of labor given the potential risk of bias in two studies and the heterogeneity in interventions. Given the inconsistency in findings the SOE Was rated as insufficient for the duration of second stage labor.

Two studies investigated lying positions using a bed with several optional adjustments (PSU bed; head and foot of bed angles, lumbar support, leg placement, etc.).[118,121] One study found statistically significant lower duration of second-stage labor in the intervention group compared with lying with the head of the bed at 45, 60, and 15 degrees,[118] and the other found significant differences between groups using the PSU bed and those in traditional beds.[121] SOE was rated as insufficient for all interventions other than ambulation during the first stage of labor.

Of the ten studies with nulliparous participants, only three reported cesarean delivery outcomes.[92,107,110] All three studies found lower numbers of cesarean deliveries in intervention groups, though only one poor quality study showed a statistically significant difference ($p<0.01$).[110] Given the potential high risk of bias, the SOE was rated as insufficient for ambulation. The SOE was rated as moderate for positioning given the consistent findings of the two included studies and the support of the meta analysis discussed below.

Maternal Outcomes for Ambulation and Positioning Strategies

Only one good-quality study reported maternal outcomes.[107] A kneeling position was associated with non-significant reductions in pelvic floor trauma (vaginal laceration, sphincter rupture, third- and fourth-degree perineal tears) (low SOE).

Neonatal Outcomes for Ambulation and Positioning Strategies

Two poor-quality studies reported neonatal outcomes. Abnormal fetal heart rate tracing data were reported without significance values in both studies.[110,119] The study using a movement intervention found 0.9% of the experimental group and 1.9% of the control group experienced abnormal fetal heart rate (FHR) tracing,[110] and a study investigating a supported sitting versus supine position showed 7 of 100 individuals in the experimental group with abnormal FHR tracing compared to 13 of 100 individuals in the control group.[119] Given the potential risk of bias in these studies the SOE was rated as insufficient.

Process-Related Outcomes for Ambulation and Positioning Strategies

Tow poor-quality studies reported on parental preferences.[110,119] In the first study,[110] in the intervention group, 23.6% of mothers rated their satisfaction level as "moderate" while 76.4% rated it as "high." In the control group, 11.4% rated satisfaction as "low," 26.7% as "moderate," and 61.9% as "high" ($p<0.01$). In comparing a supported sitting position with a supine position, 93% of those women in the sitting (experimental) group expressed a higher preference for assigned position for next childbirth, compared with 61% of women in the supine position.[110] 92% of women in the supported sitting position agreed that the assigned position was more comfortable for giving birth, compared with 54% in the supine group. In the second study,[119] 93% of women stated a higher preference of the supporting sitting position for their next childbirth, compared with 61% in the supine position. Given the high risk of bias in these two studies the SOE was rated as insufficient.

Table 34. Effects of ambulation versus control treatment

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Santhi, 2012[87] Fair	Semi-sitting position: HOB at 45° during 2nd stage labor N= 25	Supine position N=25	Mean duration of 2nd stage: 33 min (SD NR)	59 min (SD NR)	<.05	—	—	—	—	—
Thies-Lagergren, 2013[92] Fair	Birth seat N=500	Mother's choice of birth position (including birth seat)N=502	1st stage=444 min (236) 2nd stage= 38 min (25) 3rd stage= 14 min (15)	455 min (228) 44 min (27) 13 min (15)	0.494 0.001 0.620	n=23 4.6%	n=29 5.8%	0.39	Shorter 2nd stage in intervention group consistent with lower cesarean delivery rate	—
Taavoni, 2011[98] Fair	Birth ball/Peanut ball N=NR (Total N enrolled= 62)	Reclining on bed	Active phase:1.78 hr (0.58) (N=NR)	1.67 hr (0.98) (N=NR)	0.605	—	—	—	Unknown	—
Miquelutti, 2007[104] Good	Information and encouragement for upright position during 1st stage (N=54)	Free to move as desired (usual care) N=53	1st stage: Median=390 min (NR) n=35 2nd stage: 29.5 min	Median=325 min (NR) n=42 36 min	0.59 0.76	NR: only "normal delivery" reported	—	—	—	"Normal" delivery RR: Intervention 0.85 (0.63 to 1.14)
Ragnar, 2006[107] Good	Kneeling position, leaning toward HOB (N=138)	Sitting position, HOB at 60° (N=133)	2nd stage= 48.5 min (27.6) Total labor duration= 9.4 hr (5.8)	41 min (23.4) 9.1 hr (4.6)	0.017 0.64	0	2	0.15	Yes; significance NR	—

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Vaijayanthimala, 2014[110] Poor	Movement during labor (walking, rocking, swaying on a birthball, etc.) discussed/encouraged(N=106)	Control (movement during labor not discussed) (N=105)	< 12hr: 53 (50%) 12-14hr: 21 (19.8%) >14hr: 32(30.2%)	24 (22.9%) 29 (27.6%) 52 (49.5%)	0.001	14 (13.3%)	21 (21.1%)	<0.01	Yes	–
Prabhakar, 2015[113] Good	Ambulation for 1-1.5 hr with rest periods (N=30)	Confined to bed most of the time (N=30)	Duration: 575.27 min (79.33)	617.20 min (62.3)	0.027	Only "normal" vs. "abnormal" reported	–	–	–	–
Sasitorn, 2013[118] Fair	PSU birthing bed without the holding bar (N=60)	PSU birthing bed with the holding bar (N=60) Usual birthing bed with HOB at 45-60° (N=60) Usual birthing bed with HOB at 15° (N=60)	2nd stage: 17.63 min (9.70)	16.58 min (8.47) 24.18 min (14.20) 31.63 min (14.22)	<0.001	–	–	–	–	Both PSU groups had significantly lower duration of 2nd stage
Ganapathy, 2012[119] Poor	HOB elevated to 60° in 2nd stage of labor (N=100)	Flat supine (N=100)	2nd stage: 56 min	67 min	<0.05	Only "instrumental deliveries" reported	NR	NR	Unknown	–

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Phumdoung, 2007[121] Poor	PSU Cat position (alternate with high head) (N=40)	PSU Cat (alternate with supine) (N=40) High head position (N=41) Supine position (N=43)	Time in active phase: 212.38 min (114.54)	289.88 min (106.68) 208.29 min (82.10) 379.74 min (126.59)	<0.001 (between-group differences)	—	—	—	—	Music therapy group removed for N; 1 cesarean delivery in entire group (Arm NR); supine group had longer labor duration than all other groups (significance NR)

Abbreviations: Com=comparator; HOB=head of bed; Int=intervention; min=minutes; NR=not reported; NS=not significant; SD=standard deviation

Results in Women of Mixed or Unspecified Parity

Two fair-quality studies examined the effects of ambulation and positioning in populations of unclear parity. One compared a squatting position with a supine position in second-stage labor[105] and another compared use of a peanut ball after an epidural to a control group.[114]

Duration of Labor and Cesarean Delivery Rates for Ambulation and Positioning Strategies

Both studies found statistically significant reductions in duration of labor. Women using a squatting position experienced shorter second-stage labor ($p<0.05$),[105] while women using a peanut ball had reductions in duration of first and second stages of labor ($p=0.006$ and $p<0.001$, respectively).[114] Given findings from just one study regarding the first stage labor duration, the SOE was rated as insufficient. The consistent findings across the two studies resulted in a low SOE rating for the second stage labor duration outcome.

In both studies, intervention groups had lower rates of cesarean delivery, but only the peanut ball study demonstrated statistical significance ($p=0.011$) (insufficient SOE).

Maternal Outcomes for Ambulation and Positioning Strategies

One study reported data on pelvic floor trauma and hemorrhage, showing non-significant differences in periurethral tears, second- and third-degree perineal tears, and postpartum hemorrhage between groups laboring in a squatting position versus a seated position (insufficient SOE).[105]

Neonatal Outcomes for Ambulation and Positioning Strategies

Shoulder dystocia was reported for two neonates in the control group using a seated position for labor, versus no reports of shoulder dystocia in the squatting position group.[105]

Process-Related Outcomes for Ambulation and Positioning Strategies

Nonsignificant differences were reported between groups of women using a peanut ball and the control group in numbers of forceps and vacuum deliveries.[114] Eleven percent of the group using a squatting position had forceps delivery compared with 24% in the supine group ($p<0.05$) (insufficient SOE).

Relevant Systematic Reviews/Meta-Analyses for Ambulation and Positioning Strategies

We identified two good-quality SR/MAs that examined the effects of ambulation and positioning during labor on labor outcomes, with mixed parity groupings. One assessed the effects of various upright positions (including ambulation, sitting, kneeling, and standing) compared to recumbent positions (including supine).[29] Analyses of up to 11 studies indicated reduced duration of first-stage labor for women in upright positions (MD -1.43, 95% CI -2.35 to -0.50). These findings were inconsistent with our primary studies which demonstrated no difference (low SOE).

Consistent with our included studies, this meta analysis also supported no difference in cesarean delivery rates (RR 0.70, 95% CI 0.49 to 1.01) (moderate SOE). There were no significant differences for other outcomes for mothers or babies. In spite of methodological and quality heterogeneity, sensitivity analyses of higher quality studies supported the main findings.

A second review examined whether encouraging women to adopt an upright position or ambulate during first-stage labor reduced the duration of this stage.[45] Analyses of 5 studies with between 68 and 1024 participants found non-statistically significant reductions in favor of upright position/ambulation in duration of first-stage labor in nulliparous women (WMD -0.52 hours, 95% CI -2.13 to 1.09) and parous women (WMD -0.54 hours, 95% CI -1.75 to 0.671). Other outcomes, including mode of delivery, maternal, and neonatal outcomes, were not affected.

Strength of Evidence for Ambulation and Positioning Strategies

Tables 35–37 summarize the SOE for ambulation or positioning versus control therapy. Overall the SOE was reduced given the potential risk of bias in the included studies.

Table 35. Ambulation versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[110,113] (271)	**Improvement with ambulation:** 1 good-quality[113] and 1 poor-quality study[110] found that ambulation was associated with significantly reduced duration of the first stage and total duration of labor. SOE was reduced given the quality of the studies and imprecision of the findings.	Low (Medium risk of bias, indirect, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[110] (211)	**Inconclusive:** The SOE was rated as insufficient given findings from 1 study with high risk of bias.	Insufficient (High risk of bias, indirect, imprecise, 1 study)
Adverse Events			
Neonatal Outcomes – Abnormal Fetal Heart Tracing	1 RCT[110] (211)	**Inconclusive:** The SOE was rated as insufficient given findings from on1e study with high risk of bias.	Insufficient (High risk of bias, indirect, imprecise, 1 study)
Process Related Outcomes – Parental Preferences	1 RCT[110] (211)	**Inconclusive:** The SOE was rated as insufficient given findings from 1 study with high risk of bias.	Insufficient (High risk of bias, indirect, imprecise, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Table 36. Positioning versus control: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	4 RCTs[98,104,107,119] (608)	**No difference:** None of four studies examining use of a birth ball, kneeling, sitting, or semi-sitting laboring positions found statistically significant differences in duration of active labor. The SOE was reduced given the potential risk of bias and variation in interventions.	Low (High risk of bias, indirect, imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	7 RCTs[87,92,104,107,118,119,121] (2,034)	**Inconclusive:** Given the inconsistency, imprecision, and potential risk of bias, the SOE was rated as insufficient.	Insufficient (High risk of bias, indirect, Inconsistent, imprecise)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[92,107] (1,273) 1 SR[29] (2079)	**No difference:** No significant differences were found between the intervention and control groups in mode of delivery. The SOE was increased given the support of a meta analysis of 11 studies.	Moderate (Medium risk of bias, indirect, imprecise)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[107] (271)	**Improvement with kneeling:** Women in kneeling position were more likely than women in sitting position to have an intact peritoneum (51 vs. 37%) and fewer 3rd or 4th degree tears (3 vs. 6%).	Low (Imprecise, one study)
Neonatal Outcomes – Abnormal Fetal Heart Tracing	1 RCT[119] (200)	**Inconclusive:** The SOE was rated as insufficient given findings from one study with high risk of bias.	Insufficient (High risk of bias, indirect, Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Table 37. Ambulation/positioning versus control: Strength of evidence in in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[114] (201)	**Inconclusive:** SOE was insufficient given potential risk of bias and findings from 1 study.	Insufficient (Medium risk of bias, indirect, Imprecise, o1ne study)
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCT[105,114] (401)	**Improvement with positioning:** Second stage of labor was significantly shorter in women using either a peanut ball or a squatting position.	Low (Medium risk of bias, indirect, Imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[105,114] (342)	**Inconclusive:** SOE was rated as insufficient given potential risk of bias and 2 studies where only 1 demonstrated statistical significance.	Insufficient (Medium risk of bias, indirect, Inconsistent, imprecise)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[105] (200)	**Inconclusive:** SOE was insufficient given potential risk of bias and findings from 1 study.	Insufficient (Medium risk of bias, Imprecise, 1 study)
Maternal Outcomes – Hemorrhage	1 RCT[105] (200)	**Inconclusive:** SOE was insufficient given potential risk of bias and findings from 1 study.	Insufficient (Medium risk of bias, Imprecise, 1 study)
Neonatal Outcomes – Shoulder Dystocia	1 RCT[105] (200)	**Inconclusive:** SOE was insufficient given potential risk of bias and findings from 1 study.	Insufficient (Medium risk of bias, indirect, Imprecise, 1 study)
Process Related Outcomes – Mode of Delivery (Operative Vaginal Delivery)	1 RCT[114] (142)	**Inconclusive:** SOE was insufficient given potential risk of bias and findings from 1 study.	Insufficient (Medium risk of bias, indirect, Imprecise, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

10. Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations versus Control Treatment

Eight studies examined the effects of specific nutritional,[91] oral, or parenteral hydration recommendations or limitations on labor outcomes.[88,93,94,97,100,102,106] One good-quality study compared oral with parenteral hydration,[97] and another good-quality study compared combined oral and parenteral hydration to discretionary parenteral and oral hydration.[100] Two good-quality studies compared parenteral hydration of normal saline and dextrose to normal saline alone.[93,102] Three good-quality[97,100,106] and one fair-quality study[94] examined the effects of varying hydration volumes using Lactated Ringer's solution. One fair-quality study examined the effects of parenteral hydration using D5LR, a Lactated Ringer's solution containing a 5% dextrose injection.[88]

Five good-quality[93,97,100,102,106] and two fair-quality[88,94] studies examined the effects of oral and parenteral hydration recommendations and limitations on labor outcomes in nulliparous women. Table 38 shows results for these studies.

One fair-quality study examined the effects of oral carbohydrate intake on women of mixed parity.[91] Two relevant good-quality SR/MAs were identified.[31,33]

Results in Nulliparous Women

Duration of Labor and Cesarean Delivery Rates for Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations

The four studies examining the effects of intravenous hydration with a Lactated Ringer's (LR) solution were divided in significant findings.[94,97,100,106] Intravenous hydration was found to significantly decrease ($p<.001$) duration of active labor compared to oral hydration only in one fair-quality study,[94] yet had no significant effects when oral hydration was unrestricted in two good-quality studies.[97,100]

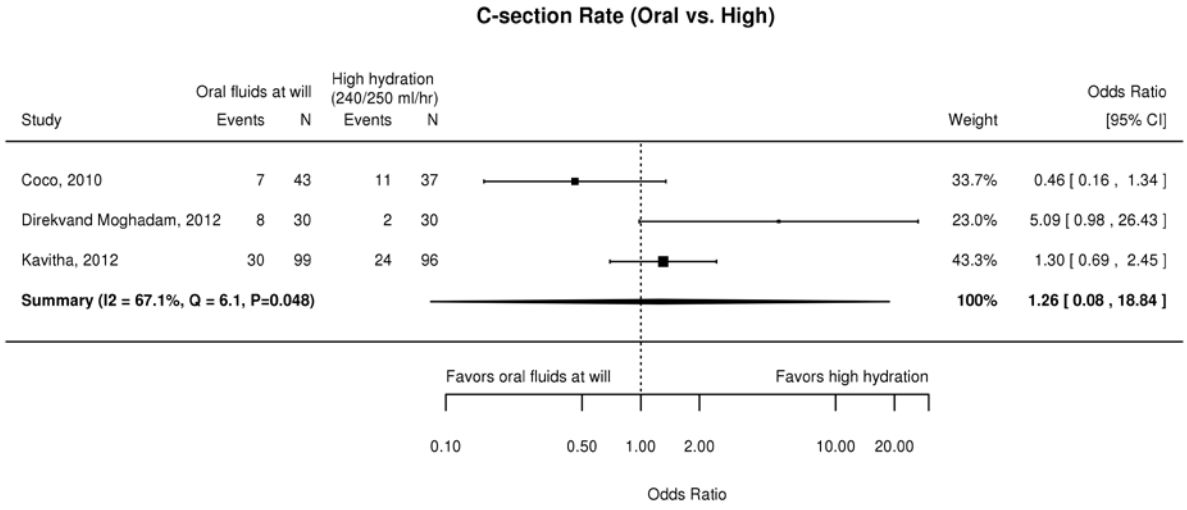
When compared with a lower volume of LR solution (125 ml/hr) in one study, a higher volume (250 ml/hr) resulted in a shorter mean duration of labor ($p=.001$).[106] Parenteral D5LR at 125 ml/hr and 250 ml/hr with limited oral intake was not found to significantly reduce labor duration compared to a rate of 25 ml/hr and ad libitum oral hydration.[88] However, a 5% intravenous dextrose (D5) solution was associated with reductions in second-stage labor ($p=0.01$) and time from fluid initiation to delivery ($p=0.02$).[102] Infusion of a dextrose and saline solution was associated with significantly decreased overall labor duration ($p=0.0$).[93] When combined with the SR evidence discussed below we rated the SOE as low for a reduction in total duration of labor. The SOE was reduced given the inconsistency in the findings from the individual trials and the variability in interventions assessed.

Six studies reported cesarean delivery rates. While infusions of LR at both 125 and 250 ml/hr did not result in significantly fewer cesarean deliveries, there was a trend in that direction with increased hydration ($p=0.1$[106]). Neither parenteral D5LR[88] nor intravenous solutions of 5% and 10% dextrose[102] resulted in significant differences in rate of cesarean delivery compared to normal saline ($p=0.309$[88] and $p=0.21$[102]). No significant differences were noted when comparing 250 ml/hr LR to unrestricted oral hydration ($p=0.30$[100]), LR at 125ml/hr, 250ml/hr, and oral hydration ($p=0.824$[97]), or LR at 60, 120, and 240 ml/hr with oral hydration ($p=0.58$[94]).

Meta-analysis of the data from three RCTs[94,97,100] with moderate heterogeneity ($I^2=67.1\%$, $Q=6.1$, $p=0.048$) showed no significant difference in cesarean delivery rates (OR 1.26, 95% CI 0.08 to 18.84) for women receiving high levels of intravenous hydration (either 240 or 250

ml/hr) compared to those with ad libitum oral hydration only (Figure 3) (moderate SOE). These findings were supported by the two SRs discussed below.

Figure 3. Forest plot of cesarean delivery rate for oral hydration versus high-level intravenous hydration



Abbreviations: CI=confidence interval

Maternal Outcomes for Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations

Two good-quality studies reported maternal outcomes. Both found that intravenous dextrose solution was not significantly associated with lower rates of chorioamniotis (infection) or postpartum hemorrhage compared to normal saline alone (p=0.2[93]; p=0.21[102]) (low SOE).

Neonatal Outcomes for Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations

One good-quality study reported neonatal outcomes. Statistical significance was not found for participants experiencing abnormal fetal heart rate tracing in one study comparing 5% and 10% dextrose solutions to normal saline (5% arm, 2/94 individuals; 10% arm, 8/98 individuals; control/normal saline arm: 2/97 individuals).[102]

Process-Related Outcomes for Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations

Five studies reported other process-related outcomes. Intravenous dextrose and normal saline solution was associated with a significantly lower number of participants experiencing prolonged labor (p=0.009) compared to normal saline alone, but not with number of operative vaginal deliveries, though intervention groups experienced fewer (p=0.1).[93] Number of operative vaginal deliveries were not significantly different between arms receiving infusions of LR at 125 or 250 ml/hr compared with unrestricted oral fluids and LR at 25 ml/hr.[88] Differences in incidence of prolonged labor were not noted when comparing intravenous LR at rates of 125 and 250 ml/hr with oral hydration.[97] No significant differences in vacuum extractions were noted with increased intravenous hydration (moderate SOE).[100,106]

Table 38. Effects of specific nutritional or oral or parenteral hydration

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Edwards, 2014[88] Fair	125 ml/hr D5LR (N=105)	250 ml/hr D5LR (N=105) 25 ml/hr D5LR (N=105)	Total duration: 11.6 hr (5.9) 1st stage: 10.2 hr (5.6)	Total duration: 11.4 hr (5.5) 1st stage: 10.3 hr (5.2) Total duration (hr): 11.5 (5.9) 1st stage (hr): 9.9 (5.7)	0.998 0.671	23	18 17	0.309 0.3605	–	–
Sharma, 2012[93] Good	NS with dextrose alternating with NS at 175 ml/hr (N=122)	NS at 175 ml/hr (N=121)	Total duration: 297.8 min (154.4)	473.8 min (220.5)	0.000	–	–	–	–	–
Direkvand-Moghadam, 2012[94] Fair	LR 60 ml/hr (N=24)	LR 120 ml/hr (N=26) LR 240 ml/hr (N=28)	Active phase of 1st phase: 237.8 min (36.4) 2nd phase: 54.8 min (16.2) 3rd phase: 6.2 min (2.9)	Active phase of 1st phase: 231.7 min (43.5) 2nd phase: 51.3 min (11.9) 3rd phase: 6.1 min (4.0) Active phase of 1st phase: 206.2 min (38.3) 2nd phase: 49.8 min (11.4) 3rd phase: 5.7 min (2.7)	0.5949 0.3857 0.9204	20	13.3 6.7	0.0167	– –	NR significant between LR arms

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
		Oral fluids at will (N=22)		Active phase of 1st phase:252.3 min (40.9) 2nd phase: 64.3 min (13.9) 3rd phase: 6.9 min (3.6)	<0.001 0.01	26.6		0.58		
Kavitha, 2012[97] Good	Oral hydration (N=99)	LR 125 ml/hr (N=98) LR 250 ml/hr (N=96)	Active labor: 391.3 min (211) Active labor (min): 343 min (171)	Active labor: 363.1 min (172)	0.203	30.6%	31% 25%	0.824	–	–
Coco, 2010[100] Good	LR 250 @ 250 ml/hr plus unrestricted oral fluids (N=37)	LR at provider's discretion plus unrestricted oral fluids (usual care) (N=43)	1st stage (mean hr; vaginal deliveries only): 7.9 2nd stage (mean hr; vaginal deliveries only):1.6 Total (mean hr; vaginal deliveries only):9.5	1st stage (mean hr; vaginal deliveries only): 8.0 2nd stage (mean hr; vaginal deliveries only):1.4 Total (mean hr; vaginal deliveries only):9.4	0.90 0.49 0.92	11	7	0.30	–	–

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Shrivastava, 2009[102] Good	5% dextrose in NS (N=76)	10% dextrose in NS (N=72) NS (control) (N=84)	Median Min from fluid initiation to complete cervical dilation: 299 (82-1091) 2nd stage: 69 (17-227) Min from fluid initiation to delivery: 392 (100-1157)	Median Min from fluid initiation to complete cervical dilation: 328 (61-672) 2nd stage: 62 (14-191) Min from fluid initiation to delivery: 393 (97-827) Min from fluid initiation to complete cervical dilation: 360 (95-1203) 2nd stage: 106 (24-266) Min from fluid initiation to delivery: 464 (185-1336)	0.1 0.01 0.02	18	24 14	0.21	–	–
Eslamian, 2006[106] Good	LR 125ml/hr (N=153)	LR 250 ml/hr (N=147)	1st stage: 367 min (105) 2nd stage: 18.52 min (10) Total: 386 min (110)	1st stage: 236 min (86) 2nd stage: 16.55 min (7) Total: 253 min (97)	0.0001 0.08 0.001	10	1	0.1	Yes. But cesarean delivery difference is NS (“trend toward a lower frequency of cesarean deliveries”)	–

Abbreviations: Com=comparator; hr=hours; Int=intervention; IQR=interquartile range; LR=Lactated Ringer’s solution; min=minutes; NS=not significant

Results in Women of Mixed or Unspecified Parity

Duration of Labor and Cesarean Delivery Rates for Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations

Oral carbohydrate intake was associated with a significant decrease in duration of second-stage labor compared to water only (p=0.04).[91] Differences in third-stage and overall duration were not statistically significant (p=0.1 and 0.3, respectively). Oral carbohydrate intake was not associated with significant differences in rates of cesarean delivery (p=0.9). These findings were all rated as insufficient SOE given imprecise findings from one fair-quality study.

Process-Related Outcomes for Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations

Oral carbohydrate intake was not associated with significant differences between rates of spontaneous, instrumental vaginal, or caesarian delivery (p=0.9) (insufficient SOE).[91]

Relevant Systematic Reviews/Meta-Analyses for Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations

We identified two good-quality SR/MAs that examined the effects of specific nutritional or oral or parenteral hydration recommendations or limitations on labor outcomes.[31,33] One investigated the harms and benefits of oral food and fluid restriction with and without intravenous hydration.[31] Analyses included 4 pertinent studies (one excluded due to including labor induction) with between 60 and 328 patients, all women with low risk of complications. No statistically significant differences were observed in cesarean delivery rates, duration of labor, or any outcomes, indicating insufficient evidence for oral fluid restrictions. The other review examined whether routine administration of intravenous fluids reduced the duration of labor or affected maternal or neonatal health.[33] Analyses of nine studies revealed some decrease in labor duration in some studies. This meta analysis included all three of our primary RCTs.[94,97,100] No differences in rate of cesarean delivery or neonatal outcomes (when reported) were noted. Heterogeneity in quality and methodology across studies precludes recommendation of routine parenteral hydration in laboring women.

Strength of Evidence for Specific Nutritional or Oral or Parenteral Hydration Recommendations or Limitations

Tables 39 and 40 summarize the SOE for nutritional, oral, or parenteral hydration interventions in nulliparous or mixed parity women.

Table 39. Specific nutritional or oral or parenteral hydration recommendations or limitations: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	3 RCTs[88,93,106] (861) 1 SR[33] (1,781)	**Improvement with intravenous fluids:** Administration of intravenous fluids compared with oral intake alone demonstrated a reduction in the duration of labor. The SOE was reduced given the inconsistency in the findings of individual trials and the variability in hydration strategies.	Low (Indirect, inconsistent, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	6 RCTs[88,94,97,100,102,106] (1,373)	**No difference:** No significant differences were found between groups of women receiving oral hydration versus high-level intravenous hydration (OR 1.26, 95% CI 0.08 to 18.84)	Moderate (Indirect, Imprecise)
Adverse Events			
Maternal Outcomes – Hemorrhage or Infection	2 RCTs[93,102] (539)	**No difference:** No significant differences in rates of maternal hemorrhage or infection were found between groups of women receiving infusions of 5% or 10% dextrose and normal saline.	Low (Imprecise)
Neonatal Outcomes – Abnormal Fetal Heart Tracing	1 RCT[102] (289)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Indirect, Imprecise, 1 study)
Process Related Outcomes – Mode of Delivery (Operative Vaginal Delivery)	5 RCTs[88,93,100,106] (1,234)	**No difference:** No difference in operative vaginal delivery rates amongst 5 studies using varying methods of hydration.	Moderate (Indirect, Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: CI=confidence interval; OR=odds ratio; RCT=randomized controlled trial; SOE=strength of evidence

Table 40. Specific nutritional or oral or parenteral hydration recommendations or limitations: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[91] (177)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study with potential risk of bias.	Insufficient (Medium risk of bias, indirect, Imprecise, 1 study)
Process Related Outcomes – Duration of Total Labor	1 RCT[91] (177)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study with potential risk of bias.	Insufficient (Medium risk of bias, indirect, Imprecise, 1 study)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[91] (177)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study with potential risk of bias.	Insufficient (Medium risk of bias, indirect, Imprecise, 1 study)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Mode of Delivery (Operative Vaginal Delivery)	1 RCT[91] (177)	**Inconclusive:** SOE was insufficient given imprecise findings from one study with potential risk of bias.	Insufficient (Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Key Question 4. Epidural Analgesia

KQ 4 was: What are the benefits and harms of epidural analgesia in labor, particularly in terms of the risk of a diagnosis of prolonged labor?

In this key question, we focus on the evidence on the effect of specific methods for analgesia during labor, particularly various approaches to regional analgesia using epidural or other methods, on the duration of labor and the risk of cesarean delivery.

Description of Included Studies

We identified 22 articles[80,124-144] representing 19 individual RCTs that examined the benefits and harms of epidural analgesia in labor. Three studies were each described in two publications, as follows:

- de Orange, 2011: Primary report[132] and a companion paper[129]
- Pascual-Ramirez, 2011: Primary report[133] and a companion paper[128]
- Wilson, 2009: Primary report[137] and a companion paper[134]

However, while the companion papers for Pascual-Ramirez, 2011, and Wilson, 2009, individually met inclusion criteria, they did not provide additional unique information on outcomes of interest to this review beyond the information provided in the primary report. The companion paper for de Orange, 2011 is cited where relevant under "Detailed Synthesis" below.

Of the 19 included studies, 8 were conducted in UK/Europe,[124-126,130,133,135,137,139] 3 were conducted in Asia,[80,143,144] 3 were conducted in the Middle East,[127,140,141] 3 were conducted in Latin America,[132,136,138] 1 was conducted in Africa,[131] and 1 was conducted in the United States.[142] Twelve studies were conducted in a hospital,[80,124,125,127,130,131,133,138,140-142,144] while 7 studies were unclear or reported other settings.[126,132,135-137,139,143] Three studies reported government funding,[80,137,141] two reported nongovernment, nonindustry funding,[140,142] and 1 reported a mixture of funding from government and nongovernment sources.[126] Thirteen studies were unclear or did not report the funding source.[124,125,127,130-133,135,136,138,139,143,144] Finally, of the 19 included studies, 7 studies were rated as good quality,[125,127,132,133,141,142,144] 9 as fair quality,[80,124,126,130,136-140] and 3 as poor quality.[131,135,143]

Comparisons of interest were:

1. Epidural analgesia versus combined spinal epidural analgesia
2. Epidural analgesia versus patient-controlled intravenous analgesia
3. Epidural analgesia versus intravascular tramadol
4. Early versus late epidural analgesia
5. Routine epidural analgesia versus analgesia on request
6. Combined spinal epidural analgesia versus nonpharmacologic pain relief

7. Epidural analgesia versus intravenous meperidine
8. Epidural analgesia versus low-dose infusion epidural analgesia
9. Epidural analgesia versus acupuncture point nerve stimulation
10. Epidural analgesia versus no epidural analgesia

Key Points for Epidural Analgesia

- For nulliparous women, a meta-analysis showed no significant differences between epidural analgesia (EA) and combined spinal epidural (CSE) in duration of the first stage of labor (low SOE) or duration of the second stage of labor (low SOE). However, total duration of labor (from time of intervention to delivery) was significantly longer for EA relative to CSE (moderate SOE). There were no differences between EA and CSE in rates of cesarean delivery (moderate SOE).
- For women of mixed parity, there was no difference between EA and CSE for total duration of labor (low SOE), or rates of cesarean delivery (moderate SOE).
- For women of mixed parity, there were no differences between EA and patient-controlled intravenous analgesia (PCIA) in duration of labor or rates of cesarean delivery (low SOE for both outcomes).
- For nulliparous women, there was no difference in duration of first or second stage labor or rates of cesarean delivery for early versus late EA (moderate SOE for all outcomes
- For women of mixed parity, there was no evidence of a difference between EA and no EA for the duration of the first stage of labor or rates of cesarean delivery. There was a slight increase in the duration of the second stage for women with EA (moderate SOE for all outcomes).

Detailed Synthesis for Epidural Analgesia

1. Epidural Analgesia versus Combined Spinal Epidural Analgesia

Of the 19 included studies, 9 RCTs representing 1,251 patients compared epidural analgesia (EA) with combined spinal epidural (CSE), which involves both epidural and spinal analgesia.[126,127,131,133,136-139,144] Of these nine RCTs, four were conducted in UK/Europe,[126,133,137,139] two were conducted in Asia or the Middle East,[127,144] and three were conducted in Latin America or Africa.[131,136,138] One RCT reported funding from a government agency,[137] one reported a mixture of funding from government and nongovernment sources,[126] and the remaining seven were unclear or did not report the funding source. Three RCTs were rated as good quality,[127,133,144] five were rated as fair,[126,136-139] and one was rated as poor quality.[131]

Of the nine RCTs that compared EA with CSE, five included only nulliparous women.[127,131,137,139,144] and one included both nulliparous and multiparous women but reported duration of labor results separately for the 52.8% of the patient population who were nulliparous.[133] The remaining three RCTs included mixed parity populations, with the following proportion of nulliparous women in each study: 68.7%,[126] 82.5%,[136] and 68.8%.[138] None of the studies reported findings specifically for multiparous women.

No SR/MAs were identified that were relevant to this comparison.

Results in Nulliparous Women

Duration of Labor and Cesarean Delivery Rates for Epidural Analgesia versus Combined Spinal Epidural Analgesia

Six of the nine RCTs that compared EA with CSE reported duration of labor,[133] cesarean delivery rates,[137] or both[127,131,139,144] in nulliparous women. Table 41 shows results for these studies; outcomes are described following the table.

Table 41. Effects of epidural analgesia versus combined spinal epidural in nulliparous women

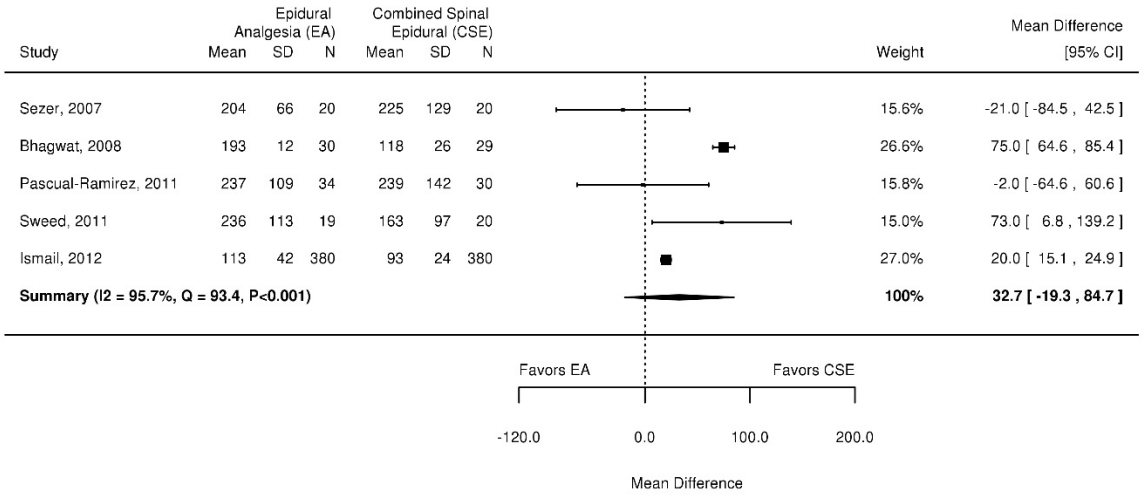
Study Quality	Int N	Com N	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?
Bhagwat, 2008[144] Good	EA 30	CSE 30	Stage 1: 193 min ± 12 Stage 2: 30 min ± 7	Stage 1: 118 min ± 26 Stage 2: 19 min ±21	Stage 1: <0.001 Stage 2: 0.409	2 (6.7%)	2 (6.7%)	1	No
Ismail, 2012[127] Good	EA 380	CSE 380	Stage 1, latent phase: 468 min ±54 Stage 1, active phase: 113 min ±42 Stage 2: 60 min ±30 Total: 648 min ±234	Stage 1, latent phase: 396 min ±42 Stage 1, active phase: 93 min ±24 Stage 2: 48 min ±18 Total: 582 min ±180	Stage 1, latent phase: <0.0001 Stage 1, active phase: <0.0001 Stage 2: <0.0001 Total: <0.0001	95 (25.0%)	87 (22.9%)	0.50	No
Pascual-Ramirez, 2011[133] Good	EA 34 33 33	CSE 30 29 29	Stage 1: 237 min ±109 Stage 2: 48 min ±32 Total: 282 min ±113	Stage 1: 239 min ±142 Stage 2: 51 min ±34 Total: 185 min ±145	Stage 1: 0.94 Stage 2: 0.76 Total: 0.91	–	–	–	No
Sezer, 2007[139] Fair	EA 20	CSE 20	Stage 1: 204 min ±66 Stage 2: 66 min ±48 Total: 270 min ±73	Stage 1: 225 min ±129 Stage 2: 56 min ±27 Total: 299 min ±138	Stage 1: 0.52 Stage 2: 0.42 Total: 0.41	4 (20.0%)	4 (20.0%)	1	No
Sweed, 2011[131] Poor	EA 20	CSE 20	Stage 1: 236 min ±113 Stage 2: 41 min ±33	Stage 1: 163 min ±97 Stage 2: 66 min ±40	Stage 1: 0.03 Stage 2: 0.049	1 (5.0%)	0 (0%)	0.31	No
Wilson, 2009[137] Fair	EA 353	CSE 351	–	–	–	98 (27.8%)	99 (28.2%)	0.91	–

Abbreviations: CI=confidence interval; Com=comparator; CSE=combined spinal epidural; EA=epidural analgesia; Int=intervention; Min=minutes; N=number of patients/participants; NR=not reported; SD=standard deviation

Five of the nine RCTs that compared EA with CSE reported either mean time from randomization or initiation of the analgesia intervention to delivery, or duration of both the first and second stages of labor[127,131,133,139,144] in nulliparous women (Table 41). Three of these RCTs were rated as good quality,[127,133,144] one as fair,[139] and one as poor.[131] These 5 RCTs represented 962 patients. Four studies included only nulliparous patients,[127,131,139,144] and one[133] reported findings for duration of labor separately for the subset of patients who were nulliparous.

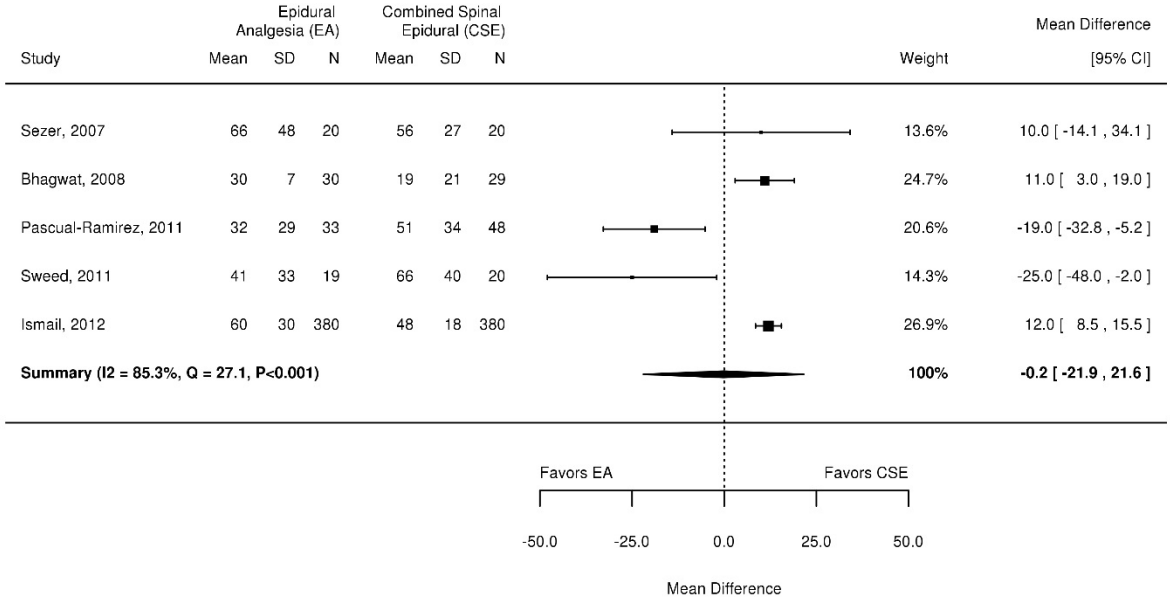
Meta-analysis of the data from these RCTs showed no significant differences between EA and CSE in duration of the first stage of labor (mean difference [MD] 32.7 minutes; 95% CI -19.3 to 84.7) (Figure 4, low SOE) or duration of the second stage of labor (MD -0.2 minutes; 95% CI -21.9 to 21.6) (Figure 5, low SOE). However, total duration of labor (from time of intervention to delivery) was significantly longer for EA relative to CSE, with an MD of 62.0 minutes (95% CI 7.2 to 116.7) (Figure 6, moderate SOE).

Figure 4. Epidural analgesia versus combined spinal epidural in nulliparous women—duration of first stage of labor



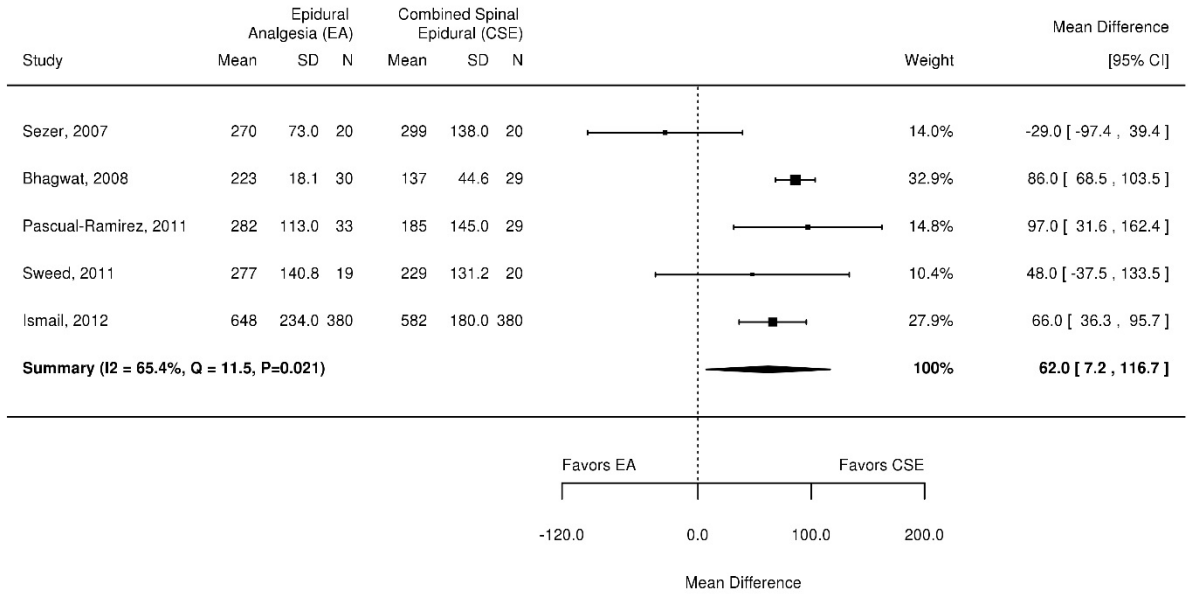
Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; N=number of participants; SD=standard deviation

Figure 5. Epidural analgesia versus combined spinal epidural in nulliparous women—duration of second stage of labor



Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; N=number of participants; SD=standard deviation

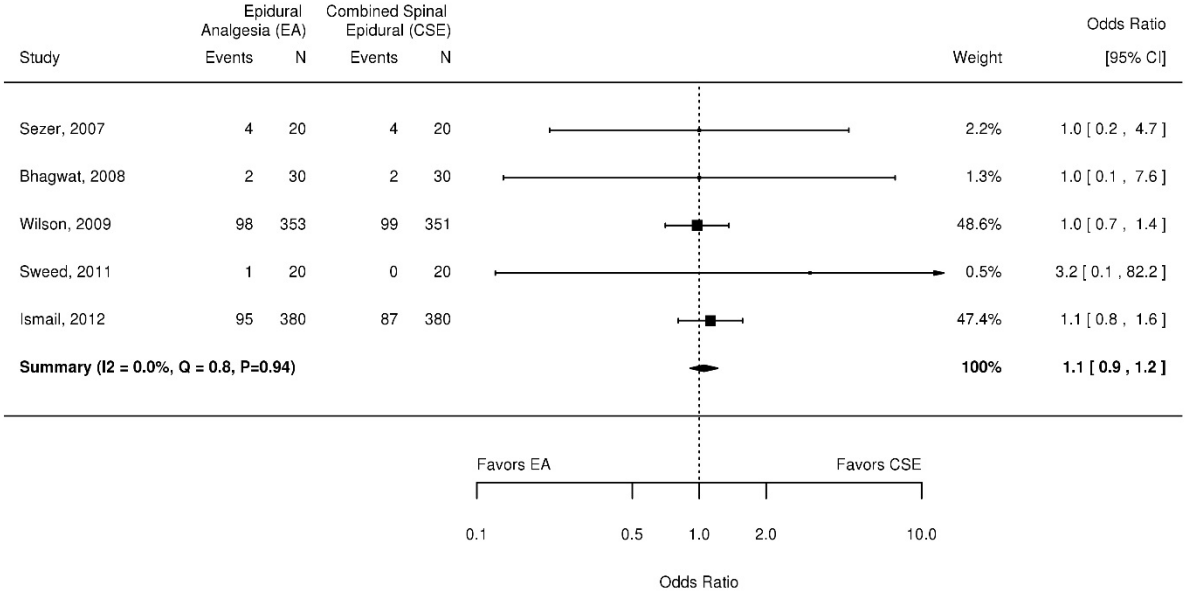
Figure 6. Epidural analgesia versus combined spinal epidural in nulliparous women—total duration of labor



Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; N=number of participants; SD=standard deviation

Five RCTs compared cesarean delivery rates associated with EA versus CSE among nulliparous women.[127,131,137,139,144] (Table 41). Two of these RCTs were rated as good quality,[127,144] two as fair,[137,139] and one as poor.[131] Meta-analysis of the data from 1604 patients in these 5 RCTs showed no statistically significant difference in cesarean delivery rates between EA and CSE (odds ratio [OR] 1.1; 95% CI 0.9 to 1.2) (Figure 7, moderate SOE).

Figure 7. Epidural analgesia versus combined spinal epidural in nulliparous women—cesarean delivery rates



Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; N=number of participants; SD=standard deviation

Process-Related Outcomes for Epidural Analgesia versus Combined Spinal Epidural Analgesia

A good-quality RCT involving 1,140 patients assessed maternal overall satisfaction with analgesia 24 hours after delivery using a using a 4-point verbal scale ranging from very satisfied to very dissatisfied (1=very dissatisfied, 2=dissatisfied, 3=satisfied, 4=very satisfied).[127] Mean maternal satisfaction scores (SD) associated with each of the 3 study interventions were 2.8 (0.8) for EA, 3.9 (0.6) for CSE, and 3.0 (0.7) for patient-controlled IV analgesia ($p<0.001$ for the 3-way comparison).

Results in Women of Mixed or Unspecified Parity

Duration of Labor and Cesarean Delivery Rates for Epidural Analgesia versus Combined Spinal Epidural Analgesia

Four RCTs compared EA with CSE in women with mixed parity. The proportion of nulliparous women in each of these studies was as follows: 68.8%,[138] 82.5%,[136] 52.8%,[133] and 68.7%.[126] Table 42 shows results for these studies; the two outcomes are described following the table.

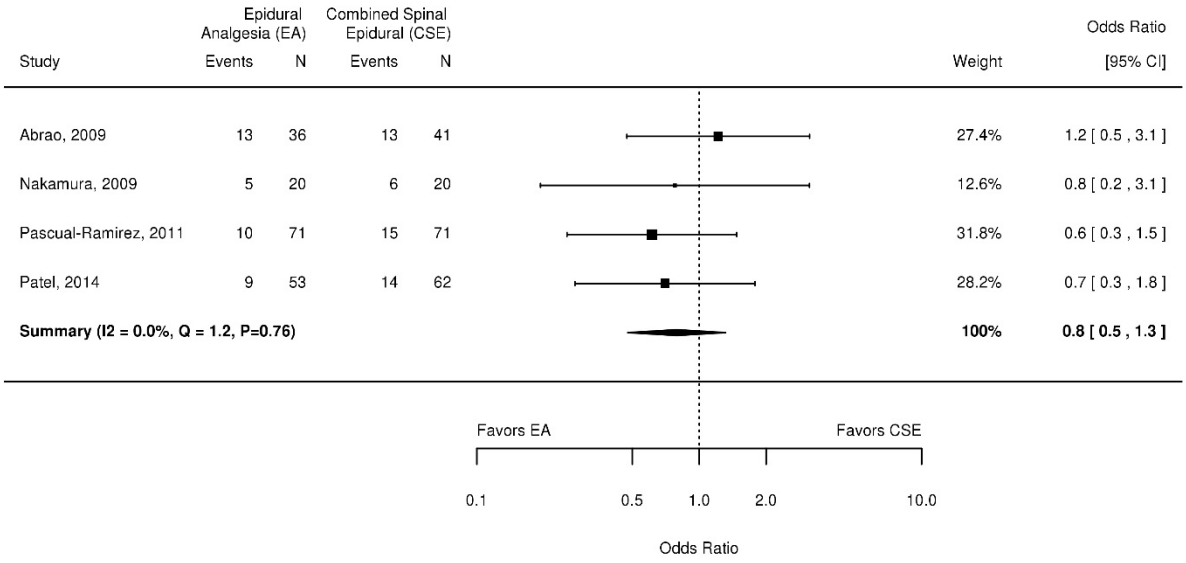
Table 42. Effects of epidural analgesia versus combined spinal epidural in women of mixed or unspecified parity

Study Quality	Int N	Com N	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?
Abrao, 2009[138] Fair	EA 36	CSE 41	–	–	–	13 (36%)	13 (32%)	0.68	No
Nakamura, 2009[136] Fair	EA 20	CSE 20	–	–	–	5 (25%)	6 (30%)	0.72	No
Pascual-Ramirez, 2011[133] Good	EA 63 62 62	CSE 58 57 57	Stage 1: 204 min ±109 Stage 2: 42 min ±32 Total: 246 min ±112	Stage 1: 212 min ±133 Stage 2: 43 min ±34 Total: 255 min ±144	Stage 1: 0.85 Stage 2: 0.60 Total: 0.77	10 (14.1%)	15 (21.1%)	0.27	No
Patel, 2014[126] Fair	EA 53	CSE 62	Total: Median 431 min (IQR 283 to 589)	Total: Median 462 min (IQR 291 to 611)	NS	9 (17.0%)	14 (22.6%)	0.45	No

Abbreviations: CI=confidence interval; Com=comparator; CSE=combined spinal epidural; EA=epidural analgesia; Int=intervention; IQR=interquartile range; Min=minutes; N=number of patients/participants; NR=not reported; SD=standard deviation

A single, good-quality study involving 144 patients of mixed parity reported duration of labor in the comparison of EA versus CSE.[133] In this study, mean duration of the first stage of labor was 204 minutes (SD=109) for EA compared with 212 minutes (SD=133) for CSE (p=0.85), and mean duration of the second stage of labor was 42 minutes (SD=32) for EA compared with 43 minutes (SD=34) for CSE (p=0.60). SOE was rated as insufficient for both outcomes. Mean time for total duration of labor was 246 minutes (SD=112) for EA, versus 255 minutes (SE=144) for CSE (p=0.77). A fair-quality study involving 115 patients also found no difference in median duration of total labor between EA and CSE (low SOE).[126] All four RCTs that compared EA with CSE in a mixed parity population reported cesarean delivery rates.[126,133,136,138] Meta-analysis of these data involving 374 patients of mixed parity generated an estimate of the odds ratio of cesarean delivery associated with CSE relative to EA of 0.8 (95% CI: 0.5 to 1.3) (Figure 8, moderate SOE).

Figure 8. Epidural analgesia versus combined spinal epidural in women of mixed or unspecified parity—cesarean delivery rates



Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; N=number of participants; SD=standard deviation

Neonatal Outcomes for Epidural Analgesia versus Combined Spinal Epidural Analgesia

Neither EA nor CSE was associated with neonatal intensive care admissions in the single, fair-quality RCT involving 115 patients that compared EA with CSE and reported this outcome (insufficient SOE).[126]

Process-Related Outcomes for Epidural Analgesia versus Combined Spinal Epidural Analgesia

CSE was found to be associated with a higher proportion of patients with abnormal fetal heart rate tracings than EA in a fair-quality RCT involving 77 patients (31.7% vs. 5.6%, respectively; p<0.01).[138] In another fair-quality RCT involving 115 patients,[126] an abnormal fetal heart tracing pattern was noted in 13% of patients in the CSE arm, compared with 6% in the EA

group. This corresponds to a risk ratio of 2.28 (95% CI 0.64 to 8.16) of CSE relative to EA (low SOE).

Another good-quality RCT involving 144 patients assessed maternal satisfaction with analgesia at three different time points: initially; during stage 1 of labor; and during stage 2 of labor.[133] The median maternal satisfaction score of 1 for initial satisfaction was statistically lower (indicating a higher level of satisfaction) for EA compared with CSE with the median score of 2 (p=0.005). There were no statistically significant between-group differences in satisfaction with analgesia during either the first or second stages of labor (insufficient SOE).

Strength of Evidence for Epidural Analgesia versus Combined Spinal Epidural Analgesia

Tables 43 and 44 summarize the SOE for the comparison of EA versus CSE. In general, meta analysis of the included studies allowed low and moderate SOE for major outcomes of interest.

Table 43. Epidural analgesia versus combined spinal epidural: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	5 RCTs[127,131,133,139,144] (1,424)	**No difference:** Meta-analysis showed no significant differences between EA and CSE in duration of the first stage of labor (mean difference [MD] 32.7 minutes; 95% CI -19.3 to 84.7).	Low (Medium risk of bias, indirect, inconsistent, imprecise)
Process Related Outcomes – Duration of 2nd Stage Labor	5 RCTs[127,131,133,139,144] (1,424)	**No difference:** Meta-analysis showed no significant differences between EA and CSE in duration of the second stage of labor (MD -0.2 minutes; 95% CI -21.9 to 21.6).	Low (Medium risk of bias, indirect, inconsistent, imprecise)
Process Related Outcomes – Total Duration of Labor	5 RCTs[127,131,133,139,144] (1,424)	**Worsening with EA:** Meta-analysis showed total duration of labor (from time of intervention to delivery) was significantly longer for EA relative to CSE, with an MD of 62.0 minutes (95% CI 7.2 to 116.7).	Moderate (Medium risk of bias, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	5 RCTs[127,131,137,139,144] (1,604)	**No difference:** Meta-analysis of the data from 1604 patients in these 5 RCTs showed no statistically significant difference in cesarean delivery rates between EA and CSE (odds ratio [OR] 1.1; 95% CI 0.9 to 1.2).	Moderate (Indirect)
Adverse Events			
Process Related Outcomes – Parental Preferences	1 RCT[127] (1,140)	**Inconclusive:** SOE was insufficient given imprecise findings from one study	Insufficient (imprecise, one study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; MD=mean difference; OR=odds ratio; RCT=randomized controlled trial; SOE=strength of evidence

Table 44. Epidural analgesia versus combined spinal epidural: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[133] (144)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study	Insufficient (Indirect, imprecise, one study)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[133] (144)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study	Insufficient (Indirect, imprecise, one study)
Process Related Outcomes – Total Duration of Labor	2 RCTs[126,133] (258)	**No difference:** No significant difference between EA and CSE for total duration of labor.	Low (Medium risk of bias, imprecise)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	4 RCTs[126,133,136,138] (374)	**No difference:** Meta-analysis generated an estimate of the odds ratio of cesarean delivery associated with CSE relative to EA of 0.8 (95% CI: 0.5 to 1.3).	Moderate (Medium risk of bias)
Adverse Events			
Neonatal Outcomes – Admission to NICU	1 RCT[126] (115)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study	Insufficient (Medium risk of bias, imprecise, one small study)
Process Related Outcomes – Abnormal Fetal Heart Tracing	2 RCTs[126,138] (190)	**Improvement with EA:** CSE was associated with a higher proportion of patients with abnormal fetal heart rate tracings than EA in one study and a risk ratio of 2.28 (95% CI: 0.64 to 8.16) for an abnormal fetal heart tracing in another study.	Low (Medium risk of bias, imprecise)
Process Related Outcomes – Parental Preferences	1 RCT[133] (142)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study	Insufficient (Imprecise, one small study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; CSE=combined spinal epidural; EA=epidural analgesia; RCT=randomized controlled trial; SOE=strength of evidence

2. Epidural Analgesia versus Patient-Controlled Intravenous Analgesia

Results for the comparison of EA and combined patient-controlled intravenous analgesia (PCIA) were reported for nulliparous women in one study[127] and for a mixed population of women in three studies.[80,130,135] We also identified one good-quality SR/meta-analysis relevant to this comparison.[28]

Results in Nulliparous Women

Duration of Labor and Cesarean Delivery Rates for Epidural Analgesia versus Patient-Controlled Intravenous Analgesia

A single, good-quality RCT conducted in Egypt compared duration of labor and cesarean delivery rates associated with EA in comparison with both PCIA with remifentanil and CSE in 1140 nulliparous women.[127] Duration of labor did not appear to be different between these two groups. Mean duration of labor in hours for EA compared with PCIA were, respectively, 10.8 (SD=3.9) versus 10.3 (SD=3.5) for total labor duration; 7.8 (SD=0.9) versus 7.7 (SD=0.8) for

duration of the latent phase of the first stage; 1.88 (SD=0.7) versus 1.80 (SD=0.6) for duration of the active phase of the first stage; and 1.0 (SD=0.5) versus 0.95 (SD=0.4) for duration of the second stage. The cesarean delivery rate was 25.0% in both groups. Given findings from one RCT in a non-U.S. setting the SOE was rated as insufficient for all outcomes.

Process-related Outcomes for Epidural Analgesia versus Patient-Controlled Intravenous Analgesia

The RCT by Ismail et al.[127] assessed maternal overall satisfaction with analgesia 24 hours after delivery was assessed using a using a 4-point verbal scale ranging from very satisfied to very dissatisfied (1: very dissatisfied, 2: dissatisfied, 3: satisfied, 4: very satisfied).[127] Statistical significance testing for the EA versus PCIA comparison was not reported, but the mean maternal satisfaction score of 2.8 (SD=0.8) for EA was similar to the satisfaction score of 3.0 (SD=0.7) for PCIA (insufficient SOE).

Results in Women of Mixed or Unspecified Parity

Three RCTs compared EA with PCIA among women with mixed or unspecified parity. One was a fair-quality study conducted in Norway involving 23 nulliparous and 16 multiparous women,[130] one was a fair-quality study conducted in China involving 120 patients of unclear parity,[80] and one was a poor-quality RCT conducted in The Netherlands involving 12 nulliparous and 14 multiparous patients.[135] Results were not reported separately by parity. Table 45 shows results for these studies**.**

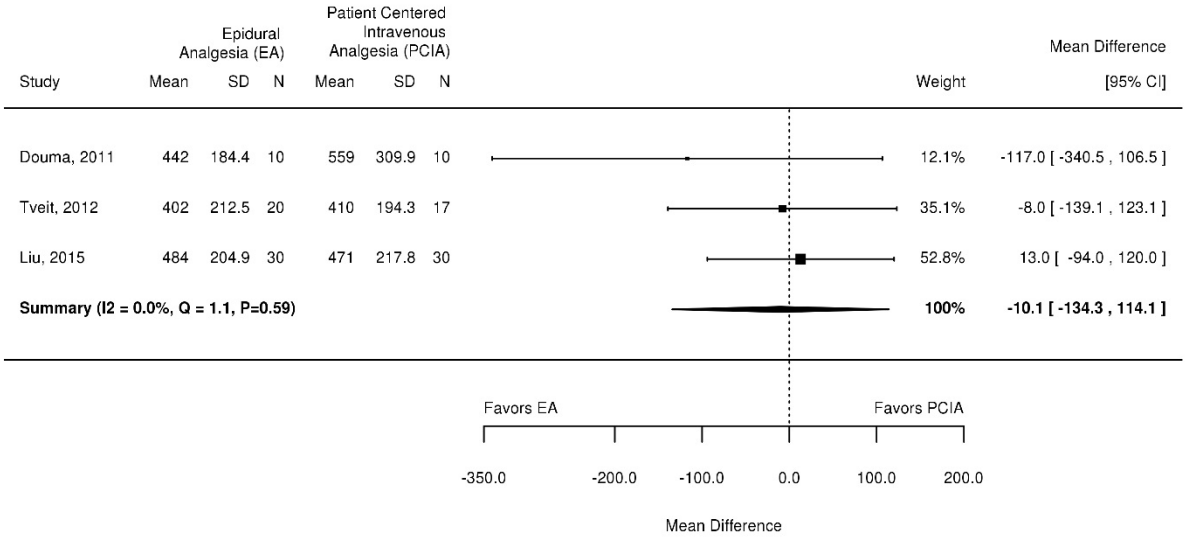
Table 45. Effects of epidural analgesia versus patient-controlled intravenous analgesia in women of mixed or unspecified parity

Study Quality	Int N	Com N	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?
Douma, 2011[135] Poor	EA 10	PCIA 10	Stage 1: 410 min ±173 Stage 2: 32 min ±14	Stage 1: 488 min ±277 Stage 2: 71 min ±40	Stage 1: 0.42 Stage 2: 0.009	2 (20%)	1 (10%)	0.53	No
Liu, 2015[80] Fair	EA N=30	PCIA 30	Stage 1: 423 min ±181 Stage 2: 61 min ±29	Stage 1: 425 min ±199 Stage 2: 46 min ±9	Stage 1: 0.97 Stage 2: 0.03	2 (6.7%)	2 (6.7%)	1	No
Tveit, 2012[130] Fair	EA 20	PCIA 17	Stage 1: 360 min ±186 Stage 2: 42 min ±32	Stage 1: 359 min ±188 Stage 2: 51 min ±34	Stage 1: 0.98 Stage 2: 0.41	3 (15.0%)	1 (5.9%)	0.37	No

Abbreviations: CI=confidence interval; Com=comparator; EA=epidural analgesia; Int=intervention; min=minutes; N=number of patients/participants; NR=not reported; NS=not statistically significant; PCIA=patient-controlled intravenous analgesia; SD=standard deviation

Meta-analysis of these 3 RCTs did not identify differences in duration of labor between these two strategies for analgesia, with the estimated mean difference in total duration of labor after EA administration minus duration after PCIA being -10.1 minutes (95% CI -134.3 to 114.1) (Figure 9). Given the potential risk of bias in all of the included studies and their non-U.S. settings, the SOE was rated as low.

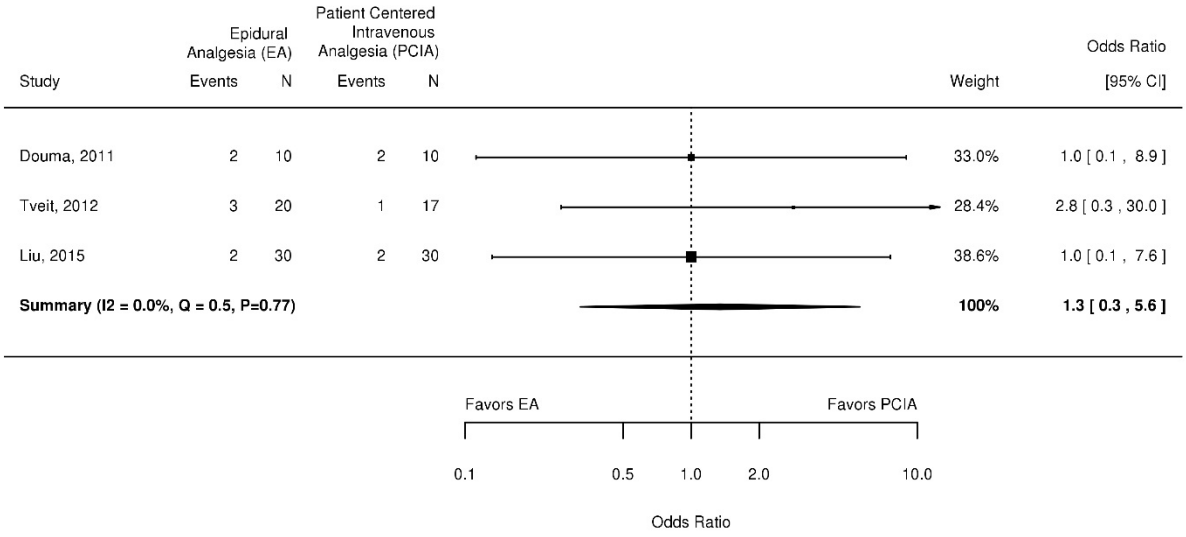
Figure 9. Epidural analgesia versus patient-controlled intravenous analgesia in women of mixed or unspecified parity—total duration of labor



Abbreviations: CI=confidence interval; EA=epidural analgesia; N=number of participants; PCIA=patient-controlled intravenous analgesia; SD=standard deviation

Meta-analysis of the three RCTs that compared EA with PCIA[80,130,135] generated an estimate of the odds ratio for cesarean delivery of EA relative to PCIA of 1.3 (95% CI 0.3 to 5.6) (Figure 10). This suggests that there is no statistically significant difference in cesarean delivery rates between these two interventions. Again given potential risk of bias, non-U.S. setting, and the imprecision of the findings the SOE was rated as low.

Figure 10. Epidural analgesia versus patient-controlled intravenous analgesia in women of mixed or unspecified parity—cesarean delivery rates



Abbreviations: CI=confidence interval; EA=epidural analgesia; N=number of participants; PCIA=patient-controlled intravenous analgesia; SD=standard deviation

Process-related outcomes for Epidural Analgesia versus Patient-Controlled Intravenous Analgesia

In the RCT by Tveit et al.,[130] abnormal fetal heart rate tracings were present in one of 20 patients in the EA group and 2 of 17 patients in the PCIA group. In the same RCT, one of 20 patients in the EA group and none of the 17 patients in the PCIA group delivered a baby with congenital hip displacement. Maternal self-reports of satisfaction with analgesia were similar between the two intervention groups. The SOE was rated as insufficient given imprecise findings in this single small study.

Relevant Systematic Reviews/Meta-Analyses for Epidural Analgesia versus Patient-Controlled Intravenous Analgesia

A good-quality SR and meta-analysis published in 2014, with a final search date of November 29, 2012, reviewed and synthesized the findings from published RCTs that compared EA with PCIA with the analgesic medication remifentanil.[28] Parity of the women included in the studies was not reported. Of the five RCTs included in that SR, three are also included in our review.[127,130,135] We excluded the remaining two studies that were included in the SR by Liu et al. because they did not report outcomes of interest and therefore the findings of the SR do not add to our included evidence and findings.

Strength of Evidence for Epidural Analgesia versus Patient-Controlled Intravenous Analgesia

Tables 46 and 47 summarize the SOE for the comparison of EA versus CSE. In general, the strength of evidence was judged insufficient for outcomes given the imprecision of the findings, findings for specific outcomes from just one study, and the non-U.S. settings. Low SOE was reported for duration of labor and cesarean delivery in women with mixed or unspecified parity.

Table 46. Epidural analgesia versus patient-controlled intravenous analgesia: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 RCT[127] (1,140)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecise, one study, non-U.S. setting)
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[127] (1,140)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecise, one study, non-U.S. setting)
Process Related Outcomes – Total Duration of Labor	1 RCT[127] (1,140)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecise, one study, non-U.S. setting)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[127] (1,140)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecise, one study, non-U.S. setting)
Adverse Events			
Process Related Outcomes – Parental Preferences	1 RCT[127] (1,140)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecise, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table 47. Epidural analgesia versus patient-controlled intravenous analgesia: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Total Duration of Labor	3 RCTs[80,130,135] (177)	**No difference:** Meta-analysis did not identify differences in duration of labor, with the estimated mean after EA administration minus duration after PCIA being -10.1 minutes (95% CI -134.3 to 114.1).	Low (Medium risk of bias, imprecise, non-U.S. settings)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	3 RCTs[80,130,135] (17)	**No difference:** Meta-analysis generated an estimate of the odds ratio for cesarean delivery of EA relative to PCIA of 1.3 (95% CI 0.3 to 5.6).	Low (Medium risk of bias, imprecise, non-U.S. settings)
Adverse Events			
Process Related Outcomes – Abnormal Fetal Heart Tracing	1 RCT[130] (37)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study performed in a non-U.S. setting.	Insufficient (Imprecise, one study, non-U.S. setting)
Process Related Outcomes – Parental Preferences	1 RCT[130] (37)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study performed in a non-U.S. setting.	Insufficient (Imprecise, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; EA=epidural analgesia; PCIA=patient-controlled intravenous analgesia; RCT=randomized controlled trial; SOE=strength of evidence

3. Epidural Analgesia versus Intravascular Tramadol

Results for this comparison were reported for women of mixed parity in one study.[143] No relevant SR/MAs were identified.

Results in Women of Mixed or Unspecified Parity

A poor-quality RCT (N=90) conducted in India compared epidural tramadol plus bupivacaine versus intravenous tramadol in a mixed parity population.[143] The only outcome of interest reported concerned parental preferences.

Process-Related Outcomes for Epidural Analgesia versus Intravascular Tramadol

The distribution of responses for parturient satisfaction ("poor," "average," "good," "excellent") favored the epidural group ($p<0.05$). Given the high risk of bias, small size, and non-U.S. setting the SOE was rated as insufficient.

Strength of Evidence for Epidural Analgesia versus Intravascular Tramadol

Table 48 summarizes the SOE for the comparison of EA versus intravascular tramadol.

Table 48. Epidural analgesia versus intravascular tramadol: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Parental Preferences	1 RCT[143] (90)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study performed in a non-U.S. setting.	Insufficient (High risk of bias, Imprecise, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

4. Early versus Late Epidural Analgesia

Results for this comparison were reported in two good-quality RCTs.[141,142] One relevant good-quality SR/meta-analysis was also identified.[44] All three of these studies focused exclusively on nulliparous women. Although the specifics of the EA protocols differed, in all studies early initiation was defined as EA initiated before the cervix was dilated to 4-5 cm.

Results in Nulliparous Women

Duration of Labor and Cesarean Delivery Rates for Early versus Late Epidural Analgesia

A good-quality RCT conducted in Israel compared early with late initiation of EA in 449 nulliparous women.[141] Early initiation of EA consisted of immediate initiation of EA at first request (< 4 cm), and late initiation consisted of delay of EA until the cervix was dilated to at least 4 cm. Mean duration (SD) of the first stage of labor from time of randomization was significantly shorter for early (5.9 hours [2.9]) vs. late (6.6 hours [3.5]; p=0.04) initiation of EA. Mean duration (SD) of the second stage of labor did not differ between early (95 minutes [59]) vs. late (105 minutes [64]; p=0.12) initiation of EA. Cesarean delivery rates did not differ between the two groups. Early initiation of EA was associated with a 13% cesarean delivery rate, compared with 11% for late initiation (p=0.77).[141]

Another good-quality RCT conducted in the United States randomly allocated 750 nulliparous women to intrathecal fentanyl (using a spinal-epidural technique) at the first request for analgesia and epidural analgesia at the second request for analgesia (early EA) versus systemic hydromorphone at the first request for analgesia and epidural analgesia at either cervical dilatation of 4.0 cm or greater or at the third request for analgesia (late EA).[142] Relative to late EA, early EA was associated with a shorter median time to vaginal delivery with a mean difference of 81 minutes (95% CI 28 to 123) and a shorter duration of the first stage of labor with a mean difference of 81 minutes (95% CI 35 to 123). Mean duration of the second stage of labor, however, did not differ between the two groups, with a mean difference of 11 minutes (95% CI -6 to 21). The cesarean delivery rate of 17.8% associated with early EA was not statistically different from the rate of 20.7% associated with late EA (p=0.31).

Relevant Systematic Reviews/Meta-Analyses for Early versus Late Epidural Analgesia

A good-quality SR published in 2007 evaluated the effects that different timing of initiation of regional analgesia has on labor outcomes in nulliparous women.[44] The review identified and included 9 eligible RCTs involving a total of 3320 patients. Meta-analysis of 8 of these RCTs involving a total of 2980 patients generated an estimated pooled OR of 1.0 (95% CI 0.82 to 1.23) for cesarean delivery for early neuraxial analgesia relative to control interventions. The duration of labor was no different between interventions. The two RCTs included in our review and summarized above were included in this SR. The remaining 7 RCTs were published prior to the earliest eligible publication date for our review. Given the overlap of this SR with our included studies, our SOE ratings emphasize the findings of the SR.

Strength of Evidence for Early versus Late Epidural Analgesia

Table 49 summarizes the SOE for early versus late epidural analgesia. The SOE was rated as moderate for all outcomes based on evidence from the SR. The SOE was lowered given that the included studies from the SR spanned 1994-2006.

Table 49. Early versus late epidural analgesia: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	1 SR[44] (6 studies, 1,739 patients)	**No difference:** No differences between early and late EA with an odds ratio of 0.95 (95% CI 0.81 to 1.10).	Moderate
Process Related Outcomes – Duration of 2nd Stage Labor	1 SR[44] (6 studies, 1,690 patients)	**No difference:** No differences between early and late EA with a weighted mean difference of 0.52 minutes (95% CI -5.03 to 6.06 minutes)	Moderate
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 SR[44] (8 studies, 2,980 patients)	**No difference:** No differences between early and late EA (odds ratio=1.00, 95% CI 0.83 to 1.21)	Moderate

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

5. Routine Epidural Analgesia versus Analgesia on Request

Results for this comparison were reported for women of mixed parity in one study.[125] No relevant SR/MAs were identified.

Results in Women of Mixed or Unspecified Parity

A good-quality RCT conducted in The Netherlands compared routine EA with analgesia on request in the form of intramuscular opiates or EA at the first or second request for pain relief after opiates.[125] Of the 233 patients randomized to routine EA and the 255 women randomized to analgesia on request, 115 (49%) and 122 (48%), respectively, were nulliparous.

Duration of Labor and Cesarean Delivery Rates for Routine Epidural Analgesia versus Analgesia on Request

Median duration of the second stage of labor did not differ between EA (20 minutes; IQR, 10 to 50) compared with analgesia on request (19 minutes; IQR, 8.0 to 45). This corresponds to a difference in means of 2.0 (95% CI -3.2 to 7.1).[125] In the EA group, 44 patients (19% of all patients randomized to EA) underwent cesarean delivery versus 39 patients in the analgesia on request group (15% of all patients randomized to analgesia on request). This corresponds to a between-group difference in percentage of 3.6 (95% CI -3.1 to 10.3).[125] Given the imprecision in findings from one study the SOE was rated as insufficient.

Maternal Outcomes for Early versus Late Epidural Analgesia

The maternal outcomes reported in this study were postpartum hemorrhage and trauma to the pelvic floor (perineal laceration). There was no difference in the percentage of patients who experienced postpartum hemorrhage of greater than 1000 mL of blood loss between women in the EA group (6.0%) versus women in the analgesia-on-request group (4.3%). This corresponds to a difference in percentage of -0.6 (95% CI -3.5 to 2.4).[125]

There was no difference in the percentage of patients who experienced third- or fourth-degree perineal laceration between women in the EA group (0.9%) versus women in the analgesia-on-request group (1.6%). This corresponds to a difference in percentage of -0.7 (95% CI -2.6 to 1.2).[125] Again the SOE was rated as insufficient given the findings from this one study.

Neonatal Outcomes for Early versus Late Epidural Analgesia

Delivery was complicated by shoulder dystocia in 5 patients (2.1%) in the EA group versus 8 patients (3.1%) in the analgesia-on-request group. This corresponds to a difference in percentage of -1.0 (95% CI: -3.8 to 1.8) (insufficient SOE).[125]

Strength of Evidence for Early versus Late Epidural Analgesia

Table 50 summarizes the SOE for early versus late epidural analgesia. The SOE was rated as insufficient for all outcomes.

Table 50. Routine epidural analgesia versus analgesia on request: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – 2nd Stage of Labor	1 RCT[125] (603)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[125] (603)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[125] (603)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Maternal Outcomes – Hemorrhage	1 RCT[125] (603)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Neonatal Outcomes – Shoulder Dystocia	1 RCT[125] (603)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

6. Combined Spinal Epidural Analgesia versus Nonpharmacologic Pain Relief

Results for this comparison were reported for women of mixed parity in one study, which was described in two papers.[129,132] No relevant SR/MAs were identified.

Results in Women of Mixed or Unspecified Parity

A good-quality RCT conducted in Brazil randomized 35 patients of mixed parity to CSE and 35 patients to only nonpharmacologic methods of pain relief during delivery. Patients in both groups received continuous support throughout labor, including assistance provided by a doula, the use of exercise balls, massage, and music therapy.[132]

Duration of Labor and Cesarean Delivery Rates for Combined Spinal Epidural Analgesia versus Nonpharmacologic Pain Relief

Median duration of the first stage of labor was significantly shorter among patients who received CSE (180 minutes; IQR, 90 to 240) versus patients who received nonpharmacologic care only (265 minutes; IQR, 160 to 365; p=0.01). Median duration of the second stage of labor was not different between CSE and nonpharmacologic care (30 minutes; IQR, 20 to 47.5 vs. 30 minutes; IQR, 20 to 50, respectively; p=0.97).[132] Of the 35 patients randomized to CSE, 4 (11%) delivered via cesarean delivery compared with 7 of 35 patients (21%) randomized to nonpharmacologic care only (p=0.23).[132] SOE was rated as insufficient for all outcomes given findings from one small study.

Process-Related Outcomes for Combined Spinal Epidural Analgesia versus Nonpharmacologic Pain Relief

This study reported two process-related outcomes, abnormal fetal heart rate tracings and maternal satisfaction. There was no between-group difference in the rate of abnormal fetal heart rate tracings (6% for CSE vs. 9% for nonpharmacologic care only; p=0.5) (insufficient SOE).

Maternal satisfaction was significantly greater for CSE than for nonpharmacologic care only, with 97% of the patients in the CSE group reporting satisfaction with the method of pain control

versus 69% in the nonpharmacologic care group (p=0.001), and 94% versus 71% (p=0.01), respectively, reporting satisfaction with delivery (insufficient SOE).[129]

Strength of Evidence for Combined Spinal Epidural Analgesia versus Nonpharmacologic Pain Relief

Table 51 summarizes the SOE for combined spinal epidural analgesia versus nonpharmacologic pain relief. The SOE was rated as insufficient for all outcomes.

Table 51. Strength of evidence for combined spinal epidural analgesia versus nonpharmacologic pain relief in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – 1st Stage of Labor	1 RCT[132] (70)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Process Related Outcomes – 2nd Stage of Labor	1 RCT[132] (70)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[132] (70)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Adverse Events			
Process Related Outcomes – Abnormal Fetal Heart Tracing	1 RCT[132] (70)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Process Related Outcomes – Parental Preferences	1 RCT[132] (70)	**Inconclusive:** SOE was insufficient given imprecise findings from one small study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

7. Epidural Analgesia versus Intravenous Meperidine

Results for this comparison were reported for nulliparous women in one study.[140] No relevant SR/MAs were identified.

Results in Nulliparous Women

A fair-quality RCT conducted in Iran randomized 395 nulliparous women to EA (n=197) or a single dose of intravenous meperidine (n=198).[140] Given findings from one study in a non-U.S. setting with medium risk of bias the SOE was rated as insufficient for all outcomes.

Duration of Labor and Cesarean Delivery Rates for Epidural Analgesia versus Intravenous Meperidine

There were no significant between-group differences (p values reported as not significant) in either the mean duration of the active phase of the first stage of labor (2.5 hours [SD 1.4] for EA versus 2.4 hours [SD 1.6] for meperidine) or the second stage of labor (1.0 hours [SD 0.7] for EA versus 0.9 hours [SD 0.7] for meperidine).[140] There were no significant between-group differences (p values reported as not significant) in rates of cesarean delivery for dystocia (4% for EA vs. 4% for meperidine) or for bradycardia (8% for EA vs. 5% for meperidine).[140]

Neonatal Outcomes for Epidural Analgesia versus Intravenous Meperidine

There were no admissions to the neonatal intensive care unit associated with either EA or meperidine.[140]

Strength of Evidence for Epidural Analgesia versus Intravenous Meperidine

Table 52 summarizes the SOE for epidural analgesia versus intravenous meperidine. The SOE was rated as insufficient for all outcomes.

Table 52. Epidural analgesia versus intravenous meperidine: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – 1st Stage of Labor	1 RCT[140] (395)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Process Related Outcomes – 2nd Stage of Labor	1 RCT[140] (395)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[140] (395)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Adverse Events			
Neonatal Outcomes – NICU Admissions	1 RCT[140] (395)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

8. Epidural Analgesia versus Low-Dose Infusion Epidural Analgesia

Results for this comparison were reported for nulliparous women in one study.[137] No relevant SR/MAs were identified.

Results in Nulliparous Women

A fair-quality RCT conducted in the UK randomized 1052 nulliparous women to EA (n=253), CSE (n=351), or low dose infusion EA (n=350) to allow for ambulation during labor.[137] Results for the comparison of EA versus low-dose infusion EA are reported below. Cesarean delivery rate was the only outcome of interest reported. Given the imprecise findings from only one study performed in a non-U.S. setting the SOE was rated as insufficient.

Cesarean Delivery Rates for Epidural Analgesia versus Low-Dose Infusion Epidural Analgesia

Rates of cesarean delivery did not appear to differ between EA (27%) and low-dose infusion EA (29%) (p value not reported).[137]

Strength of Evidence for Epidural Analgesia versus Low-Dose Infusion Epidural Analgesia

Table 53 summarizes the SOE for epidural analgesia versus low-dose infusion epidural analgesia. The SOE was rated as insufficient for all outcomes.

Table 53. Epidural analgesia versus low-dose infusion epidural analgesia: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[137] (1,052)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

9. Epidural Analgesia versus Acupuncture Point Nerve Stimulation

Results for this comparison were reported for women of unspecified parity in one study.[80] No relevant SR/MAs were identified.

Results in Women of Mixed or Unspecified Parity

In a fair-quality RCT conducted in China, 120 patients of unspecified parity were randomized to EA (n=30), PCIA (n=30), acupuncture point nerve stimulation (n=30), or no analgesia (n=30).[80] Results for the comparison of EA versus acupuncture point nerve stimulation are reported below. Given findings from one small study in non-U.S. setting, the SOE was rated as insufficient for all outcomes.

Duration of Labor and Cesarean Delivery Rates for Epidural Analgesia versus Acupuncture Point Nerve Stimulation

Mean duration (SD) of the first stage of labor associated with EA was 423 minutes (181) compared with 430 minutes (120) for acupuncture point nerve stimulation. Mean duration (SD) of the second stage of labor was 61 minutes (29) for EA versus 43 minutes (18) for acupuncture point nerve stimulation. Statistical significance testing for these two comparisons was not reported.[80] Two of the 30 patients (6.7%) randomized to receive EA delivered via cesarean delivery, compared with 1 of the 30 patients (3.3%) in the acupuncture point nerve stimulation group (p value not reported).[80]

Maternal Outcomes for Epidural Analgesia versus Acupuncture Point Nerve Stimulation

The only maternal outcome reported in this study was postpartum hemorrhage. The mean volume of postpartum blood loss (SD) was estimated to be 125 mL (24) for the patients in the EA group, compared with 127 mL (23) in the acupuncture point nerve stimulation group (p value not reported).[80]

Neonatal Outcomes for Epidural Analgesia versus Acupuncture Point Nerve Stimulation

Neonatal hypoxia (not described further in the original report) occurred in 1 of 30 patients (3.3%) in the EA group and 2 of 30 (6.7%) in the acupuncture point nerve stimulation group (p value not reported).[80]

Strength of Evidence for Epidural Analgesia versus Acupuncture Point Nerve Stimulation

Table 54 summarizes the SOE for epidural analgesia acupuncture point nerve stimulation. The SOE was rated as insufficient for all outcomes.

Table 54. Epidural analgesia versus acupuncture point nerve stimulation: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – 1st Stage of Labor	1 RCT[80] (120)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Process Related Outcomes – 2nd Stage of Labor	1 RCT[80] (120)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[80] (120)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Adverse Events			
Maternal Outcomes – Hemorrhage	1 RCT[80] (120)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)
Neonatal Outcomes – Hypoxia	1 RCT[80] (120)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting.	Insufficient (Imprecision, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

10. Epidural Analgesia versus No Epidural Analgesia

Results for this comparison were reported for nulliparous women in one study[124] and for women of unspecified parity in another.[80] One relevant good-quality SR/meta-analysis that included studies of both nulliparous and multiparous women was identified.[38]

Results in Nulliparous Women

A fair-quality RCT conducted in Turkey randomly allocated 50 nulliparous patients each to vaginal delivery with EA (bupivacaine and fentanyl) or with no EA (1% lidocaine).[124] Three patients in the EA group and 2 in the no-EA group underwent cesarean delivery and were thus excluded from the study. Duration of labor was the only outcome of interest reported.

Duration of Labor for Epidural Analgesia versus No Epidural Analgesia

Mean duration (SD) of the active phase of the first stage of labor was significantly shorter in the EA group (218 minutes [166]) than in the no-EA group (259 minutes [158]; p=0.048).

However, mean duration of the second stage of labor was significantly longer in the EA group (29.6 minutes [43.0]) than in the no-EA group (24.8 minutes [35.3]; p=0.043).[124] Given findings from one study in a non-U.S. setting with medium risk of bias, the SOE was rated as insufficient.

Results in Women of Mixed or Unspecified Parity

In a fair-quality RCT conducted in China, 120 patients of unspecified parity were randomized to EA (n=30), PCIA (n=30), acupuncture point nerve stimulation (n=30), or no analgesia (n=30).[80] In this section we focus only on the EA versus no EA groups.

Duration of Labor and Cesarean Delivery Rates for Epidural Analgesia versus No Epidural Analgesia

Mean duration (SD) of the first stage of labor associated with EA was 423 minutes (181), compared with 440 minutes (200) for no analgesia (p=0.73). Mean duration (SD) of the second stage of labor was 61 minutes (29) for EA versus 46 minutes (21) for no analgesia (p=0.02).[80] Two of the 30 patients (6.7%) randomized to receive EA delivered via cesarean delivery, compared with 8 of the 30 patients (27%) in the no-analgesia group (p=0.036).[80]

Maternal Outcomes for Epidural Analgesia versus No Epidural Analgesia

The only maternal outcome reported in this study was postpartum hemorrhage. The mean volume of postpartum blood loss (SD) was estimated to be 125 mL (24) for the patients in the EA group, compared with 140 mL (29) in the no-analgesia group (p=0.03).[80]

Neonatal Outcomes for Epidural Analgesia versus No Epidural Analgesia

Neonatal hypoxia (not described further in the original report) occurred in 1 of 30 patients (3.3%) in the EA group and 2 of 30 (6.7%) in the no analgesia group (p=0.55).[80]

Relevant Systematic Reviews/Meta-Analyses for Epidural Analgesia versus No Epidural Analgesia

A good-quality SR published in 2011 summarized and synthesized data from eligible RCTs that compared EA with non-epidural analgesia or no analgesia in labor.[38] The authors of that review identified and included 38 studies involving 9,658 patients of mixed parity. Neither of the two RCTs that compared EA with no analgesia that met our eligibility criteria were included in this SR because of publication date eligibility criteria. Similar to our included study, results of MAs reported in this SR suggest that relative to non-epidural analgesia or no analgesia in labor, the duration of the first stage of labor associated with EA is not significantly longer (MD 18.51 minutes, 95% CI -12.91 to 49.42), but that the duration of the second stage of labor is slightly longer with EA (MD 13.66 minutes, 95% CI 6.67 to 20.66). Different from our included study, the pooled RR for cesarean deliveries associated with EA relative to nonepidural or no analgesia was estimated to be 1.10 (95% CI 0.97 to 1.25) demonstrating no difference. These findings are from studies with mixed parity.

Strength of Evidence for Epidural Analgesia versus No Epidural Analgesia

Tables 55 and 56 summarize the SOE for outcomes comparing epidural analgesia versus no epidural analgesia. The SOE was rated as moderate for major outcomes of labor duration and cesarean delivery based on the findings from a large SR.

Table 55. Epidural analgesia versus no epidural analgesia: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – 1st Stage of Labor	1 RCT[124] (100)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting with medium risk of bias.	Insufficient (Medium risk of bias, imprecision, one study, non-U.S. setting)
Process Related Outcomes – 2nd Stage of Labor	1 RCT[124] (100)	**Inconclusive:** SOE was insufficient given imprecise findings from one study performed in a non-U.S. setting with medium risk of bias.	Insufficient (Medium risk of bias, imprecision, one study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table 56. Epidural analgesia versus no epidural analgesia: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – 1st Stage of Labor	1 RCT[80] (120) 1 SR[38] (11 studies 2981 patients)	**No difference:** No evidence of a significant difference between EA and no EA (MD 18.51 minutes, 95% CI -12.91 to 49.42)	Moderate
Process Related Outcomes – 2nd Stage of Labor	1 RCT[80] (120) 1 SR[38] (13 studies 4233 patients)	**Worsening with EA:** Women with epidural analgesia had a statistically significant longer second stage of labor (average MD 13.66 minutes, 95% CI 6.67 to 20.66).	Moderate
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[80] (120) 1 SR[38] (27 studies 8417 patients)	**No difference:** No evidence of a significant difference in the risk of caesarean section overall (RR 1.10, 95% CI 0.97 to 1.25).	Moderate
Adverse Events			
Maternal Outcomes – Hemorrhage	1 RCT[80] (120)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study performed in a non-U.S. setting with medium risk of bias.	Insufficient (Medium risk of bias, imprecision, 1 study, non-U.S. setting)
Neonatal Outcomes – Hypoxia	1 RCT[80] (120)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study performed in a non-U.S. setting with medium risk of bias.	Insufficient (Medium risk of bias, imprecision, 1 study, non-U.S. setting)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; EA=epidural analgesia; MD=mean difference: RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence; SR=systematic review

Key Question 5. Frequency of Cervical Examination

KQ 5 was: How does the frequency of cervical examination affect the probability of specific benefits and harms?

Description of Included Studies

We identified no RCTs and only one good-quality SR[145] that met the inclusion criteria for this KQ. The focus of the SR was to compare different methods of assessing labor progression through the use of vaginal examinations. The objective was to compare digital vaginal examinations for assessing progress of labor to other strategies or different timings.

Key Points for Frequency of Cervical Examination

- There was insufficient SOE for all outcomes regarding the frequency of cervical examination.

Detailed Synthesis for Frequency of Cervical Examination

We identified one good-quality SR[145] which included two studies comparing the effects of vaginal examinations versus other strategies or different timings on the progression of labor and maternal and neonatal health outcomes. Only one of the studies included was relevant to this KQ: an RCT of 150 women undergoing routine vaginal examinations every 2 hours compared to every 4 hours.[146] The authors of the SR considered this study to be of poor quality due to the lack of description regarding allocation concealment in the randomization process and participants being excluded from the study after randomization who developed exclusion criteria prior to labor. The included study did not meet our inclusion criteria due to date of publication (1996).

The main outcomes were mode of birth, length of labor, incidence of maternal or neonatal infection requiring antibiotics, maternal satisfaction with intrapartum care, and hemorrhage. There was no difference between every-2-hour and every-4-hour examinations for cesarean deliver (RR 0.77; 95% CI, 0.36 to 1.64), spontaneous vaginal birth (RR 0.98; 95% CI, 0.80 to 1.21), and operative vaginal birth (RR 1.44; 95% CI, 0.66 to 3.17). The mean difference in length of labor was -6.00 minutes (95% CI, -88.70 to 76.70). There were no data on the incidence of maternal or infant infection requiring antibiotics or maternal satisfaction in labor (SOE insufficient for all outcomes).

Strength of Evidence for Frequency of Cervical Examination

Table 57 summarizes the SOE for the findings described above. All outcomes had insufficient SOE.

Table 57. Vaginal examination versus other strategies: Strength of evidence in women of unspecified parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	1 SR/MA[145] (150)	**Inconclusive:** SOE was insufficient given evidence from 1 older poor-quality study with imprecise findings.	Insufficient (High risk of bias, Imprecise, 1 study)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 SR/MA[145] (150)	**Inconclusive:** SOE was insufficient given evidence from 1 older poor-quality study with imprecise findings.	Insufficient (High risk of bias, Imprecise, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Key Question 6. Intrauterine Pressure Catheters

KQ 6 was: What are the benefits and harms of intrauterine pressure catheters in the diagnosis and management of labor dystocia?

Description of Included Studies

We did not identify any RCTs that met the inclusion criteria for this KQ. Below we describe results from one good-quality SR that addressed the benefits and harms of intrauterine pressure catheters in the diagnosis and management of labor dystocia.[32]

Key Points for Intrauterine Pressure Catheters

- There were no statistically significant differences between intrauterine pressure catheters and external uterine monitoring for the outcomes of mode of delivery, mean time to delivery, neonatal acidemia, or admission to the NICU (moderate SOE for all outcomes).

Detailed Synthesis for Intrauterine Pressure Catheters

A good-quality SR included 3 good-quality RCTs comparing the use of intrauterine pressure catheters versus external monitoring in women being induced or augmented in labor. One study (n=150) was restricted to women in spontaneous labor with a diagnosis of dystocia while the other two included both augmented and induced labors; one of these reported results by indication for oxytocin (500 women were augmented). We summarize here the pooled subgroup analyses for this population. The primary studies were not included in our review because of date of publication.

Maternal outcomes included the process outcomes of mode of delivery and duration of labor in addition to risk of infection. In the pooled analyses, internal monitoring increased the proportion of operative vaginal deliveries (OR 1.25, 95% CI 1.02 to 1.53); cesarean delivery rates were also higher with internal monitoring, but not significantly (OR 1.25, 95% CI 0.91 to 1.21) Of note, there was statistically significant evidence of heterogeneity in results comparing the augmented to the induced subgroups. There was no significant difference in the mean time to delivery in women with augmented labor who had an intrauterine pressure catheter (296.84 minutes) versus external fetal monitoring (297.19 minutes) in the one study that reported this outcome (p=0.99); median times to delivery in both studies were also similar. There were no differences for signs of infection in labor for women with internal versus external tocodynamometry (RR 0.69; 95% CI, 0.44 to 1.08).

Neonatal outcomes were not reported for the relevant subgroups.

Strength of Evidence for Intrauterine Pressure Catheters

Table 58 summarizes the SOE for the findings described above. The SOE was rated as moderate for all outcomes assessed given consistent findings from good-quality RCTs.

Table 58. Intrauterine pressure catheters versus external monitoring: Strength of evidence in women of unspecified parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Total Labor	1 SR/MA[32] of 1 RCT (1456)	**No difference:** No differences in mean time to delivery with intrauterine pressure catheters compared to external monitoring	Moderate (Indirect)
Process Related Outcomes – Mode of Delivery	1 SR/MA[32] of 2 RCTs (750)	**No difference:** Comparing intrauterine pressure catheters to external monitoring, there was no difference in delivery by operative vaginal delivery (RR 1.25, 95% CI 0.91 to 1.73) or by cesarean deliver (RR 1.25, 95% CI 0.91 to 1.71).	Moderate (Indirect)
Adverse Events			
Maternal Outcomes – Infection	1 SR/MA[32] of 1 RCTs (1456)	**No difference:** No differences in signs of infection in labor in women with intrauterine pressure catheters compared to external monitoring (RR 0.69, 95% CI 0.44 to 1.08).	Moderate (Indirect)
Neonatal Outcomes – Acidemia	1 SR/MA[32] of 1 RCT (1456)	**No difference:** No differences in neonatal acidemia (pH<7.15) in infants of women with intrauterine pressure catheters compared to external monitoring (RR 1.31, 95% CI 0.95 to 1.79).	Moderate (Indirect)
Neonatal Outcomes – Admission to NICU	1 SR/MA[32] of 2 RCTs (489)	**No difference:** No differences in admission to NICU in infants of women with intrauterine pressure catheters compared to external monitoring (RR 0.34, 95% CI 0.07 to 1.67).	Moderate (Indirect)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: CI=confidence interval; NICU=neonatal intensive care unit; RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence; SR/MA=systematic review/meta-analysis

Key Question 7. High-Dose versus Low-Dose Oxytocin Protocols

KQ 7 was: For women with abnormal labor, what are the relative benefits and harms of high- versus low-dose oxytocin protocols (including nipple stimulation).

In this key question, we review the evidence on the effect on specific approaches to oxytocin augmentation, including dose, method of administration (pulsatile vs. continuous), and timing of administration relative to phase of labor.

Description of Included Studies

We identified eight articles[73,76,147-152] representing seven individual RCTs that examined the benefits and harms of high- versus low-dose oxytocin protocols for women with abnormal labor. Of the seven included studies, five were conducted in UK/Europe,[147-149,151,152] one was conducted

in Asia,[76] and one was conducted in the Middle East.[73] All seven studies were conducted in a hospital setting. Four studies reported government funding,[147-149,151] one reported nongovernment, nonindustry funding,[152] and two were unclear or did not report the funding source.[73,76] Finally, of the seven included studies, six were rated as good quality[73,76,147,148,151,152] and one was rated as fair quality.[149]

In addition to the above studies, five good-quality SRs that addressed the benefits and harms of high-dose/low-dose oxytocin protocols are also discussed below.[153-157]

Key Points for High-Dose versus Low-Dose Oxytocin Protocols

- High-dose oxytocin is associated with a lower cesarean delivery rate compared with low-dose oxytocin protocols (moderate SOE).
- Early administration of oxytocin is associated with a shorter duration of labor (high SOE) but does not affect the overall cesarean delivery rate compared with delayed administration (high SOE). There are no difference in adverse events.
- Pulsatile administration of oxytocin is associated with a longer duration of labor compared with continuous administration (low SOE).
- There is no difference in cesarean delivery rate between women managed with oxytocin compared to expectant management (low SOE).

Detailed Synthesis for High-Dose versus Low-Dose Oxytocin Protocols

High-dose versus Low-dose Oxytocin Infusions

Two RCTs[76,147] and two SR/MAs[153,156] addressed high-dose versus low-dose oxytocin protocols for women with abnormal labor. Two RCTs[149,151] and two SR/MAs[154,157] addressed the timing of oxytocin augmentation following a diagnosis of abnormal labor. One RCT[148] studied the effect of pulsatile oxytocin infusions and another[152] the use of adjuvant beta-blockade with oxytocin. One SR/MA studied the effect of oxytocin augmentation with regional analgesia,[155] and one SR/MA[154] and one RCT[73] compared oxytocin with no oxytocin in women with abnormal labor.

High-dose versus Low-dose Oxytocin for Abnormal Labor

Oxytocin is a peptide and powerful uterotonic agent that is synthesized in the hypothalamus and secreted in a pulsatile fashion from the posterior pituitary. The synthetic version of oxytocin, pitocin, is identical to the naturally-occurring hormone and is commonly used in obstetrics for induction and augmentation of labor. Due to its short serum half-life and narrow therapeutic range, oxytocin is given as a continuous intravenous infusion and begun at a low rate and then incrementally increased until a regular contraction pattern is achieved. Intravenous oxytocin dosing protocols are typically classified as either low-dose or high-dose based on the initial starting dose and by the interval dose increase (Table 59).[158]

Table 59. Low-dose and high-dose oxytocin infusion protocols

Regimen	Starting Dose (mU/min)	Incremental Increase (mU/min)	Dosage Interval (min)
Low-dose	0.5-2	1-2	15-40
High-dose	6	3-6	15-40

Abbreviations: mU/min=milliunits per minute; min=minutes

Two RCTs and two SR/MAs addressed oxytocin dosing protocols for labor augmentation. Somprasit et al.[76] conducted an RCT of 960 nulliparous women in Thailand comparing active management versus conventional management of labor for women in spontaneous labor. The active management included early rupture of the membranes and a high-dose oxytocin infusion protocol (starting at 6 mU/min, increasing by 2 mU/min every 30 minutes to a maximal rate of 40 mU/min or to five contractions in 10 minutes). The specifics of the low-dose oxytocin protocol were not provided. There was no difference in mode of delivery, indication for cesarean or rates of maternal fever or chorioamnionitis between the two groups. Women receiving the high-dose oxytocin protocol had a shorter duration of the first stage of labor but no difference in the duration of the second stage of labor compared with women receiving the conventional protocol (Table 60).

Kenyon et al.[147] conducted a pilot RCT of high-dose oxytocin compared with a standard protocol among nulliparous women in the UK with spontaneous onset of labor and labor-complicated by dystocia. Consistent with the other RCT, there were no differences in mode of delivery or indication for cesarean delivery between the two groups. The goal of the pilot RCT was to determine if recruitment was feasible in conducting a larger trial among women in labor (Table 60).

Two SR/MAs analyzed the effect of high-dose oxytocin protocols on labor outcomes among women with dystocia. Wei et al.[156] conducted a SR/meta-analysis of 10 studies including 5423 women with labor dystocia. The studies included both nulliparous and parous women, though results were not stratified by parity. High-dose oxytocin was associated with an overall lower risk for cesarean delivery and associated higher rate of spontaneous vaginal delivery. High-dose oxytocin was associated with lower rates of labor duration greater than 12 hours but higher rates of uterine tachysystole. There were no differences in the rate of postpartum hemorrhage, need for maternal transfusion, uterine atony, uterine rupture, shoulder dystocia, chorioamnionitis, nonreassuring fetal heart rate tracings, fetal distress, meconium aspiration, neonatal acidemia, or maternal satisfaction were seen between the two groups (Table 60).

Finally, Kenyon et al. conducted a Cochrane review[153] addressing high-dose versus low-dose oxytocin protocols for augmentation of abnormal labor. Their review included 4 studies with 644 subjects. High-dose oxytocin was associated with a lower overall cesarean delivery rate and with a higher rate of spontaneous vaginal delivery and shorter duration of labor. Subgroup analysis based on parity demonstrated that lower cesarean delivery rates were seen only in multiparous women, while nulliparous women had lower but nonsignificant cesarean delivery rates. One of the four studies was judged to be at high risk of bias. When that study was removed from the analysis, the overall cesarean delivery rate among all subjects was no longer significantly different between the two oxytocin-dosing protocols. There were no differences in maternal satisfaction, chorioamnionitis, postpartum hemorrhage, emergent delivery for nonreassuring fetal status, or neonatal acidemia between the two oxytocin-dosing protocols (Table 60).

Table 60. Labor outcomes by high- and low-dose oxytocin protocols

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Somprasit, 2005[76] Good	Early AROM, 2-hour vaginal exams with high-dose oxytocin given if dilated <1 cm	No protocol for initiating/ stopping oxytocin, vaginal exams as indicated	First stage: 538.0 min (242.9)	First stage: 589.4 min (263.8)	0.0036	38/320 (11.9%)	94/640 (14.7%)	0.23	Trend toward lower cesarean delivery rate with shorter labor	Low-resource setting
Kenyon, 2013[147] Good	High-dose oxytocin	Low-dose oxytocin	–	–	–	17/47 (36.2%)	15/47 (31.9%)	0.66	–	–
Wei, 2010 (SR)[156] Good	High-dose oxytocin	Low-dose oxytocin	Labor duration >12 hr: 75/741 (10.1%)	Labor duration > 12 hr: 156/763 (20.4%)	RR 0.46 (0.30 to 0.70)	361/2748 (13.1%)	405/2675 (15.1%)	RR 0.85 (0.75-0.97)	Yes	–
Kenyon, 2013 (SR)[153] Good	High-dose oxytocin	Low-dose oxytocin	Oxytocin to delivery: 7.8 hr (2.7)	Oxytocin to delivery: 11.3 hr (6.1)	Mean difference: -3.50 hr (-6.38 to -0.62)	Overall (all subjects): 43/320 (13.4%) Overall (nulliparous): 30/138 (21.7%) Overall (multiparous): 8/82 (9.7%)	Overall (all subjects): 71/324 (21.9%) Overall (nulliparous): 48/162 (29.6%) Overall (multiparous) 14/62 (22.6%)	Overall (all subjects): RR 0.62 (0.44 to 0.86) Overall (nulliparous): RR 0.71 (0.47 to 1.06) Overall (multiparous): RR 0.43 (0.19 to 0.97)	Yes	–

Abbreviations: AROM=artificial rupture of membranes; Com=comparator; hr=hours; Int=intervention; min=minutes; RR=relative risk; SR=systematic review

Timing of Oxytocin Administration

Two RCTs[149,151] and two good-quality SR/MAs[154,157] addressed the timing of oxytocin augmentation following a diagnosis of abnormal labor. Dencker et al.[149] conducted an RCT of early (following no progress 1 hour after amniotomy, oxytocin infusion was administered within 20 minutes) versus delayed (postponement of oxytocin augmentation for 3 hours) oxytocin administration for augmentation of labor in nulliparous women. The study was conducted at 2 sites in Sweden and included 630 women. There were no significant differences in mode of delivery between the two groups, but early administration of oxytocin was associated with a shorter duration of labor from randomization to delivery. There were no differences in duration of the second stage of labor or rates of postpartum hemorrhage, need for transfusion, anal sphincter laceration, or neonatal acidosis between the two groups (Table 61).

Hinshaw et al.[151] conducted an RCT of early (within 20 minutes of randomization) versus delayed (withheld for a period of 8 hours unless intervention became clinically indicated) oxytocin administration for labor augmentation in nulliparous women. The study was conducted at 12 sites in the UK and included 412 women. There were no differences in rates of cesarean delivery between the two groups, but again duration of labor from randomization to delivery was shorter in the early oxytocin group. There were no differences in the rates of postpartum hemorrhage, need for transfusion, neonatal death or infection, or maternal satisfaction between the two groups (Table 61).

Wei et al.[157] conducted a meta-analysis on early oxytocin administration for augmentation of labor that included 9 studies and 1983 women. Early oxytocin augmentation was defined as immediate oxytocin administration when dystocia was identified. The studies included both nulliparous and parous women, though results were not stratified by parity. Early administration of oxytocin was associated with a higher rate of spontaneous vaginal delivery but similar to our included RCTs no differences in rate of cesarean delivery or operative vaginal delivery. Early administration was associated with uterine tachysystole, but there were no differences in the duration of labor (admission to delivery) or rates of postpartum hemorrhage, need for transfusion, maternal fever or chorioamnionitis, or fetal distress (Table 61).

Bugg et al. conducted a Cochrane review[154] addressing early versus delayed (delayed use by one hour or more) administration of oxytocin for labor augmentation. They identified 8 studies including 1388 women. The studies included both nulliparous and multiparous women, though results were not stratified by parity. Both our included RCTs were also included in this SR. Early administration of oxytocin was associated with a shorter duration of labor from randomization to delivery, but there were no differences in mode of delivery or rates of uterine tachysystole, postpartum hemorrhage, or maternal satisfaction between the two groups (Table 61).

Table 61. Labor outcomes by timing of oxytocin administration

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Dencker, 2009[149] Fair	Early administration of oxytocin	Delayed administration of oxytocin	Random-ization to delivery: 5.2 hr (2.8) Second stage: 1.7 hr (1.2)	Random-ization to delivery: 6.7 hr (3.2) Second stage: 1.8 hr (1.3)	Randomization to delivery: p<0.001 Second stage: p=0.68	Overall: 29/314 (9.2%)	Overall: 34/316 (10.8%)	Overall: RR 0.8 (0.5 to 1.4)	No	–
Hinshaw, 2008[151] Good	Early administration of oxytocin	Delayed administration of oxytocin	Random-ization to delivery: 5 hr 52 min (IQR 3:52 to 8:02)	Random-ization to delivery: 9 hr 8 min (IQR 5:06 to 13:16)	P<0.001	Overall: 28/208 (13.5%) NRFHT: 4/208 (1.9%) Delay: 21/208 (10.1%)	Overall: 28/204 (13.7%) NRFHT: 6/204 (2.9%) Delay: 17/204 (8.3%)	Overall: RR 0.98 (0.6 to 1.7) NRFHT: Not provided but NS Delay: RR 1.23 (0.6 to 2.4)	No	–
Wei, 2009[157] Good	Early administration of oxytocin	Delayed administration of oxytocin	–	–	Admission to delivery: Mean difference -1.36 hr (-2.82 to 0.09)	Overall: 153/1010 (15.1%)	Overall: 167/973 (17.2%)	Overall: RR 0.87 (0.71 to 1.06)	No	–
Bugg, 2013[154] Good	Early administration of oxytocin	Delayed administration of oxytocin	Randomization to delivery: 5.26 hr (0.89)	Randomization to delivery: 7.50 hr (1.39)	Randomization to delivery: Mean difference -2.20 hr (-3.29 to -1.10)	Overall: 74/610 (12.1%)	Overall: 76/590 (12.9%)	Overall: RR 0.88 (0.66 to 1.19)	No	–

Abbreviations: Com=comparator; hr=hours; Int=intervention; IQR=interquartile range; RR=relative risk

Pulsatile Oxytocin Administration and Adjuvants to Oxytocin

Endogenous oxytocin is released in a pulsatile fashion from the pituitary gland. In contrast, pitocin is most commonly given as a continuous intravenous infusion for both induction and augmentation of labor. Tribe et al.[148] conducted an RCT of pulsatile versus continuous oxytocin for augmentation of labor. The trial was conducted at two sites in the UK and included 500 women. The trial included both nulliparous and multiparous women and results were not stratified by parity. Pulsatile oxytocin was associated with longer duration of labor compared with continuous infusion. Fewer women delivered vaginally within 24 hours in the pulsatile group, but overall cesarean delivery rates were not reported. There was no difference in the rate of neonatal infection, hypoxic ischemic encephalopathy or neonatal seizures between the two groups (Table 62).

Labor is a high catecholamine state and endogenous catecholamines may interfere with uterine contractility as beta2-adrenergic receptor agonists are known tocolytic agents. Palomaki et al.[152] conducted an RCT of combined propanol (beta adrenergic receptor antagonist) plus oxytocin compared with oxytocin alone for augmentation of labor. The trial was conducted at a single site in Finland and included 107 women. Both nulliparous and parous women were included and the results were not stratified by parity. There were no differences in mode of delivery or duration of labor between the two groups (Table 62).

Table 62. Labor outcomes with pulsatile oxytocin or with adjuvants

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Tribe, 2012[148] Good	Pulsatile oxytocin	Continuous oxytocin	Infusion to delivery: 9.61 hr (95% CI 8.95 to 10.27) First and second stage of labor: 15.79 hr (95% CI 14.93 to 16.65)	Infusion to delivery: 7.17 hr (95% CI 6.58 to 7.77) First stage and second stage of labor: 14.06 hr (95% CI 13.20 to 14.92)	Infusion to delivery: RR 2.4 (1.6 to 3.3) First and second stage of labor: RR 1.7 (0.5 to 2.9)	Failed vaginal delivery by 24 hours: 119/251 (47.4%)	Failed vaginal delivery by 24 hours: 93/249 (37.3%)	Failed vaginal delivery by 24 hours: 1.27 (1.03 to 1.56)	Unknown	Overall cesarean delivery rates were not reported in the study.
Palomki, 2006[152] Good	Oxytocin plus propranolol	Oxytocin alone	Duration of augmented labor: 185 min Total duration of labor (first, second and third stage): 810 min	Duration of augmented labor: 223 min Total duration of labor (first, second, third stage): 768 min	Duration of augmented labor: p=0.217 Total duration n of labor (first, second, third stage): p=0.486	Overall: 6/55 (10.9%)	Overall: 2/52 (3.8%)	Overall: p=0.154	No	–

Abbreviations: CI=confidence interval; Com=comparator; hr=hours; Int=intervention; min=minutes; RR=relative risk

Oxytocin versus Expectant Management

Nachum et al.[73] conducted an RCT comparing various methods for labor augmentation. They included three intervention arms: amniotomy alone, amniotomy with oxytocin, and oxytocin alone. The control arm included expectant management. The results of the amniotomy and amniotomy plus oxytocin augmentation compared with expectant management are presented in KQ 2. There was no difference in mode of delivery, duration of the first stage of labor, duration of the second stage of labor, or rates of postpartum hemorrhage, anal sphincter laceration or postpartum fever between women receiving oxytocin alone compared to women in the expectant management group. Women managed with oxytocin had greater mean satisfaction scores compared with the expectantly managed group (4.7 [0.6] vs. 5.0 [0.1], $p<0.05$ after post-hoc testing) on a five-point scale from absolutely not satisfied (1) to absolutely satisfied (5). The study included both nulliparous and parous women and results were not stratified by parity.

Two SRs addressed oxytocin expectant for augmentation of labor.[154,155] One review was in the setting of concomitant regional analgesia[155] and the other was a Cochrane review on the effect of oxytocin augmentation versus expectant management for labor dystocia.[154] Costley et al. performed a SR/meta-analysis of oxytocin augmentation versus expectant management in women with epidural analgesia.[155] The review included two studies involving 319 nulliparous women. There were no differences in mode of delivery of rates of postpartum hemorrhage between the two groups. Bugg et al. conducted a Cochrane review that included 8 studies with 1388 subjects on the use of oxytocin versus expectant management for labor dystocia as well as the use of early or delayed oxytocin administration.[154] The studies included both nulliparous and parous women and results were not stratified by parity. Of the eight studies, three (138 subjects) compared oxytocin administration with expectant management. There was no difference in cesarean delivery or operative vaginal delivery between the two groups (Table 63).

Table 63. Labor outcomes with oxytocin compared to expectant management

Study Quality	Int	Com	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Costley, 2012[155] Good	Oxytocin augmentation	No intervention/ Expectant management	–	–	–	–	–	Overall: RR 0.95 (0.42 to 2.12)	–	Women with epidural analgesia
Bugg, 2013[154] Good	Oxytocin augmentation	No intervention/ Expectant management	–	–	–	Overall: 8/65 (12.3%)	Overall: 10/73 (13.7%)	Overall: RR 0.84 (0.36 to 1.96)	–	–
Nachum, 2010[73] Good	Oxytocin augmentation	No intervention/ Expectant management	Random-ization to delivery: 494 min (327) First stage: 463 min (313) Active phase: 103 min (89) Second stage: 31 min (46)	Random-ization to delivery: 498 min (306) First stage: 460 min (285) Active phase: 127 min (96) Second stage: 38 min (54)	Random-ization to delivery: p=0.94 First stage: p=0.95 Active phase: p=0.12 Second stage: p=0.41	Overall: 2/72 (2.8%)	Overall: 1/70 (1.4%)	Overall: p=0.9	No	–

Abbreviations: Com=comparator; hr=hours; Int=intervention; RR=relative risk

Strength of Evidence for High-Dose versus Low-Dose Oxytocin Protocols

Tables 63–68 summarize the SOE for the findings described above. In general, outcomes were rated as insufficient SOE except where existing SRs were able to add to the evidence base.

Table 64. High-dose versus low-dose oxytocin protocols: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 1st Stage Labor	2 RCTs[76,147] (1,052)	**Inconclusive:** SOE was insufficient given imprecise and inconsistent findings from 2 studies.	Insufficient (Inconsistent, imprecise, non-U.S. setting)
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[76,147] (1,020)	**Inconclusive:** SOE was insufficient given imprecise and inconsistent findings from 2 studies.	Insufficient (Inconsistent, imprecise, non-U.S. setting)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 RCTs[76,147] (1,052) 2 SRs[153,156] (9 studies, 945 patients)	**Improvement with high-dose oxytocin:** High- dose oxytocin augmentation was associated with a reduction in the risk of cesarean section supported by 2 RCTs and 2 SRs. There was however inconsistency in findings and substantial heterogeneity reducing the SOE.	Moderate (imprecise)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[147] (92)	**Inconclusive:** SOE was insufficient given imprecise and finding from 1 small pilot study	Insufficient (imprecise, non-U.S. setting, 1 small study)
Maternal Outcomes – Infection	2 RCTs[76,147] (1,052)	**No difference:** A small, pilot RCT demonstrated no difference in the rate of maternal infection by oxytocin dosing protocol. A good-quality RCT in Thailand showed no difference in the rate of maternal infection between high-and low-dose oxytocin as part of an active management of labor protocol compared to a conventional management of labor protocol.	Low (Imprecise)
Maternal Outcomes – Hemorrhage	1 RCT[147] (92)	**Inconclusive:** SOE was insufficient given imprecise and finding from 1 small pilot study.	Insufficient (imprecise, non-U.S. setting, 1 small study)
Neonatal Outcomes – Respiratory Distress	1 RCT[147] (92)	**Inconclusive:** SOE was insufficient given imprecise and finding from 1 small pilot study.	Insufficient (imprecise, non-U.S. setting, 1 small study)
Neonatal Outcomes – Neonatal Length of Stay	1 RCT[147] (92)	**Inconclusive:** SOE was insufficient given imprecise and finding from 1 small pilot study.	Insufficient (imprecise, non-U.S. setting, 1 small study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Table 65. Early versus delayed oxytocin protocols: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Labor	2 SR[154,157] (10 studies, 2583 patients)	**Improvement with early oxytocin:** Reduction in the overall duration of labor between women managed with early versus delayed oxytocin administration.	High
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	2 SR[154,157] (10 studies, 2583 patients)	**No difference:** No differences in rates of cesarean delivery between women managed with early versus delayed oxytocin administration (RR 0.88, 95% CI 0.66 to 1.19)	High
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	1 RCT[149] (630)	**No difference:** An RCT of nulliparous women with prolonged labor from 2 delivery units in Sweden demonstrated no differences in perineal lacerations between women managed with early versus delayed oxytocin administration.	Low (Imprecise)
Maternal Outcomes – Transfusion	2 RCTs[149,151] (1,042)	**No difference:** 2 RCTs, 1 from the UK and 1 from Sweden both each demonstrated no differences in rates of maternal transfusion between women managed with early versus delayed oxytocin administration.	Moderate
Maternal Outcomes – Hemorrhage	2 RCTs[149,151] (1,042)	**No difference:** 2 RCTs, 1 from the UK and 1 from Sweden both each demonstrated no differences in rates of maternal postpartum hemorrhage between women managed with early versus delayed oxytocin administration.	Moderate
Neonatal Outcomes – Neonatal Infection/Sepsis	1 RCT[151] (412)	**No difference:** An RCT of nulliparous women with dysfunctional labor from 12 delivery units in the UK demonstrated no differences in rates of neonatal infection/sepsis between women managed with early versus delayed oxytocin administration.	Low (1 study)
Neonatal Outcomes – Neonatal Acidemia	1 RCT[149] (630)	**No difference:** An RCT of nulliparous women with prolonged labor from two delivery units in Sweden demonstrated no differences in neonatal acidemia between women managed with early versus delayed oxytocin administration.	Low (1 study)
Process Related Outcomes – Mode of Delivery (Instrumental Delivery)	2 RCTs[149,151] (1,042)	**No difference:** 2 RCTs, 1 from the UK and 1 from Sweden both each demonstrated no differences in rates of operative vaginal delivery between women managed with early versus delayed oxytocin administration.	Moderate
Process Related Outcomes – Mode of Delivery (Spontaneous)	2 RCTs[149,151] (1,042)	**No difference:** 2 RCTs, one from the UK and one from Sweden both each demonstrated no differences in rates of spontaneous vaginal delivery between women managed with early versus delayed oxytocin administration.	Moderate

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: RCT=randomized controlled trial; RR=relative risk; SOE=strength of evidence; SR=systematic review

Table 66. Pulsatile versus continuous oxytocin protocols: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	1 RCT[148] (487)	**No difference:** No difference in the duration of the second stage of labor among women managed with pulsatile compared to continuous oxytocin for augmentation of labor.	Low (Indirect, Imprecise)
Process Related Outcomes – Duration of Labor	1 RCT[148] (481)	**Improvement with continuous oxytocin:** Women managed with pulsatile compared to continuous oxytocin for augmentation of labor had a longer duration of labor.	Low (Indirect, imprecise)
Adverse Events			
Process Related Outcomes – Mode of Delivery (Operative delivery)	1 RCT[148] (500)	**No difference:** No difference in operative delivery rate between women managed with pulsatile compared to continuous oxytocin for augmentation of labor. The cesarean delivery rate was not reported.	Low (Indirect, imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table 67. Oxytocin versus oxytocin plus other protocols: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Labor (from intervention to delivery)	1 RCT[152] (99)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 small study.	Insufficient (Imprecise, 1 small study)
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[152] (107)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 small study.	Insufficient (Imprecise, 1 small study)
Adverse Events			
Process Related Outcomes – Mode of Delivery (Instrumental Delivery)	1 RCT[152] (107)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 small study.	Insufficient (Imprecise, 1 small study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Table 68. Oxytocin versus expectant management: Strength of evidence in women of mixed parity

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of Labor (from intervention to delivery)	1 RCT[73] (99)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 small study.	Insufficient (Imprecise, 1 small study)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[73] (99) 1 SR[154] (3 studies, 138 patients)	**No difference:** No difference in cesarean delivery rate between women managed with oxytocin compared to expectant management. SOE was increased to low given findings from SR which also found no difference in cesarean delivery rates.	Low (Imprecise)
Adverse Events			
Process Related Outcomes – Mode of Delivery (Instrumental Delivery)	1 RCT[73] (99) 1 SR[154] (3 studies, 138 patients)	**No difference:** No difference in operative vaginal delivery rate between women managed with oxytocin compared to expectant management.	Low (Imprecise)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.
Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence; SR=systematic review

Key Question 8. Electronic Fetal Monitoring versus Intermittent Auscultation

KQ 8 was: For women in spontaneous labor undergoing augmentation with oxytocin, what are the relative benefits and harms (in terms of both maternal and neonatal outcomes) of electronic fetal monitoring versus intermittent auscultation?

Description of Included Studies

We were unable to identify any relevant RCTs that met our inclusion criteria at this time. We identified 4 potential SRs that had comparisons of electronic fetal monitoring to intermittent auscultation,[26,46,50,51] but these were ultimately excluded because the included studies in the reviews utilized interventions which are not currently used in the United States.

Key Question 9. Timing of Pushing in the Second Stage

KQ 9 was: For women in the second stage of labor, is there a benefit from delayed or Valsalva pushing for time to delivery or mode of delivery?

Description of Included Studies

We identified three articles[159-161] representing two individual RCTs that examined pushing techniques among 425 nulliparous women. One fair-quality RCT was conducted in the UK/Europe[159] and the other good-quality RCT was conducted in the United States.[160,161] Both studies reported conducting the trials in a hospital setting as well as reported government funding.

Key Points for Timing of Pushing in the Second Stage

- There is insufficient evidence on whether instruction on Valsalva pushing shortens the duration of the second stage of labor in nulliparous women when compared with instruction to push spontaneously or without coaching.
- Valsalva/coached and spontaneous/uncoached pushing have similar risks of trauma to the pelvic floor (low SOE).

- There was no evidence comparing the timing of pushing (immediate versus delayed) or Valsalva pushing versus spontaneous pushing in multiparous women.

Detailed Synthesis for Timing of Pushing in the Second Stage

Coached Pushing versus Uncoached Pushing

Results for this intervention were reported for nulliparous women in two studies.[159,160] No relevant SR/MAs were identified.

Results in Nulliparous Women

Two RCTs compared pushing techniques (coached/Valsalva pushing versus spontaneous or uncoached pushing) among nulliparous women without epidural analgesia.

Duration of Labor and Cesarean Delivery Rates for Coached Pushing versus Uncoached Pushing

One study[159] demonstrated a statistically significant increase in the length of the second stage of labor in women randomized to Valsalva pushing (40.8 vs. 50.1 minutes, p=0.045) (Table 69). The cesarean delivery rate for women after randomization was not reported for this study. In contrast, the other study[160] demonstrated that coached/Valsalva technique was associated with a shorter duration of the second stage compared with uncoached pushing (spontaneous or Valsalva) (59.1 vs. 46.3 minutes, p=0.014). There was no significant difference in rate of cesarean deliveries in this study. SOE was rated as insufficient for both outcomes given inconsistent and imprecise findings.

Table 69. Duration of labor and cesarean delivery rates for spontaneous pushing versus valsalva pushing

Study Quality	Int	Comp	Duration of Labor: Int	Duration of Labor: Com	Duration of Labor: P Value	Cesarean: Int	Cesarean: Com	Cesarean: P Value	Shorter Labor Associated with Lower Cesarean Delivery Rate?	Comments
Yildirim, 2008[159] Fair	Valsalva Pushing N=50	Spontaneous Pushing N=50	Duration 50.1 min ±26.3	Duration 40.8 min ±19.1	0.045	–	–	–	Unknown	–
Bloom, 2006[160] Good	Coached Pushing N=163	Un-coached Pushing N=157	Duration 46.3 min ±41.5	Duration 59.1 min ±49.1	0.014	1 (<1%)	5 (3%)	0.109	No	–
Schaffer, 2005[161]	Coached N=67	Un-coached N=61	Prolonged second stage n=3 (4%)	Prolonged second stage n=5 (8%)	0.385	–	–	–	NA	All patients had vaginal delivery

Abbreviations: Com=comparator; Int=intervention; min=minutes; NR=not reported; RR=relative risk

Maternal Outcomes for Coached Pushing versus Uncoached Pushing

While evidence is limited, there was no statistically significant increase in the incidence of maternal adverse outcomes including forceps delivery or perineal lacerations (Table 70).[159,160] The companion study also showed no difference in the incidence of urodynamic stress incontinence (low SOE).[161] There were no data on hemorrhage, maternal infection, or maternal satisfaction.

Table 70. Maternal adverse outcomes for spontaneous pushing versus valsalva pushing

Study Quality	Intervention	Comparator	Outcome	Results: Intervention	Results: Comparator	P Value
Yildirim, 2008[159] Fair	Valsalva Pushing N=50	Spontaneous Pushing N=50	2nd Degree Cervical tear	6 (12%) 2 (4%)	4 (8%) 0 (0%)	0.167 0.495
Bloom, 2006[160] Good	Coached Pushing N=163	Uncoached Pushing N=157	Forceps 3rd Degree 4th Degree	6 (4%) 12 (7%) 6 (4%)	7 (5%) 13 (8%) 2 (1%)	0.725 0.73 0.087
Schaffer, 2005[161] Good	Coached N=67	Uncoached N=61	Forceps Episiotomy 3rd or 4th degree Urodynamic stress incontinence	2 (3%) 15 (22%) 2 (3%) 11 (16%)	3 (5%) 13 (21%) 5 (8%) 7 (12%)	0.573 0.883 0.195 0.443

Neonatal Outcomes for Coached Pushing versus Uncoached Pushing

While evidence is limited, there was no statistically significant difference between groups in the risk of fetal heart rate abnormalities, assisted respiration, acidemia, respiratory distress, sepsis evaluation, or stillbirth.[159,160] Given the imprecise findings and the small numbers of events the SOE was rated as insufficient.

Strength of Evidence for Coached Pushing versus Uncoached Pushing

Table 71 summarizes the SOE for the findings described above. In general, SOE was judged insufficient for all outcomes, with the exception of the maternal outcome of trauma to the pelvic floor.

Table 71. Spontaneous pushing versus valsalva pushing: Strength of evidence in nulliparous women

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Intermediate or Final Outcomes			
Process Related Outcomes – Duration of 2nd Stage Labor	2 RCTs[159-161] (420)	**Inconclusive:** SOE was insufficient given inconsistent and imprecise findings from 2 studies.	Insufficient (Medium risk of bias, inconsistent, imprecise)

Outcome	Study Design (Sample Size)	Conclusion	SOE (Rationale)[a]
Process Related Outcomes – Mode of Delivery (Cesarean Delivery)	1 RCT[160] (320)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Imprecise, 1 study)
Adverse Events			
Maternal Outcomes – Trauma to the Pelvic Floor	2 RCTs[159-161] (420)	**No difference:** Two RCTS reported no difference in the risk of trauma to the pelvic floor between Valsalva/coached and spontaneous/uncoached pushing strategies.	Low (Medium risk of bias, Imprecise)
Neonatal Outcomes – Neonatal Acidemia	1 RCT[160] (320)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Imprecise, 1 study)
Neonatal Outcomes – Respiratory Distress	1 RCT[160] (320)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Imprecise, 1 study)
Neonatal Outcomes – Neonatal Infection/Sepsis	1 RCT[160] (320)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Imprecise, 1 study)
Neonatal Outcomes – Long Term Health	1 RCT[160] (320)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Imprecise, 1 study)
Process Related Outcomes – Mode of Delivery (Instrumental Delivery)	1 RCT[160] (320)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Imprecise, 1 study)
Process Related Outcomes – Mode of Delivery (Spontaneous)	1 RCT[160] (320)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Imprecise, 1 study)
Process Related Outcomes – Abnormal Fetal Heart Tracing	1 RCT[159] (100)	**Inconclusive:** SOE was insufficient given imprecise findings from 1 study.	Insufficient (Medium risk of bias, imprecise, 1 study)

[a] Criteria for downgrading SOE is described as Rationale; when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Abbreviations: RCT=randomized controlled trial; SOE=strength of evidence

Discussion

In this comparative effectiveness review, we reviewed 105 studies described in 111 publications relevant to criteria used to define protracted or arrested labor (KQ 1); the benefits and harms of amniotomy (KQ 2), supportive care measures (KQ 3), and epidural analgesia (KQ 4) in spontaneous labor; the benefits and harms of cervical examination frequency (KQ 5) and intrauterine pressure catheters (KQ 6) in diagnosis and management of abnormal labor; the benefits and harms of high- and low-dose (including nipple stimulation) oxytocin augmentation in women diagnosed with abnormal labor progression (KQ 7); the benefits and harms of electronic fetal monitoring versus intermittent auscultation in women undergoing oxytocin augmentation (KQ 8); and the benefit of delayed or Valsalva pushing during the second stage of labor (KQ 9).

Key Findings and Strength of Evidence

Our review included 111 articles (105 unique studies). This included 12 studies relevant to defining abnormal labor, 8 studies relevant to amniotomy, 50 studies relevant to supportive care measures, 22 studies relevant to epidural analgesia, 1 study relevant to cervical examination, 1 study relevant to intrauterine pressure catheters, 12 studies relevant to high-dose versus low-dose oxytocin protocols, 0 studies relevant to fetal monitoring strategies, and 2 studies relevant to timing of pushing in the second stage. Evidence suggests that the duration and pattern of "normal" labor progress based on modern management is quite different than historical data, and that labor progress is different in nulliparous compared to parous women. Use of partograms did not impact important maternal or neonatal outcomes, although the applicability of this evidence to modern U.S. settings is limited. Routine amniotomy decreases the total duration of labor in nulliparous women without affecting other outcomes (moderate SOE), while routine amniotomy with oxytocin augmentation as needed decreased duration of labor without increasing cesarean delivery (high SOE). Although supportive care therapies are often seen as benefiting parental satisfaction with the birthing process, these outcomes were rarely assessed in clinical trials meeting our inclusion criteria, although an existing systematic review of 11 studies did find that women receiving continuous emotional support were less likely to rate their birth experience negatively. Of the different types of supportive therapies, only emotional support interventions showed reductions in cesarean (low SOE for doula support, moderate SOE for continuous emotional support) and instrumental deliveries (moderate SOE). For women choosing analgesia, type (epidural vs. combined spinal epidural, or epidural vs. patient-controlled intravenous analgesia) or timing during labor did not affect cesarean delivery rates (moderate SOE).

Findings in Relationship to What is Already Known

In general, the findings of the review were consistent with current understanding of the overall strength of evidence for different strategies for management of labor. Estimates of the rate of progress of "normal" labor derived from contemporary data in the United States are quite different from the classic curves described by Friedman.[14] These differences may be attributable to a number of factors, including secular trends in patient characteristics (e.g., increasing age at first birth and increasing rates of obesity) and increasing use of interventions such as induction of labor or the use of oxytocin to augment labor. More recent data suggest that the transition to active labor occurs later in the course of labor than originally described, which is reflected in

more recent guidelines suggesting a higher threshold for observing labor duration before intervention with cesarean delivery.

The definition of "normal" labor is fundamental in evaluating the evidence related to managing "abnormal" labor progression, analogous to the threshold value used to define "normal" for a continuous laboratory value. The sensitivity and specificity of the test will vary depending on the choice of threshold, but so will the estimates of the effectiveness of interventions based on that threshold. Comparing results across studies requires a common definition for such "normal" labor and permeates our review.

There is evidence that partograms are useful in low-resource settings, but they have not been shown to improve labor outcomes in high-resource settings. This may be due in part to differences in the data sources for generating labor curves and thresholds.

In general, our findings regarding other interventions are consistent with current guidelines [3], which are largely informed by the CSL data and encourage allowing longer durations for both first and second stages of labor before intervening with cesarean delivery. Routine amniotomy is not specifically recommended, although the recommendations note that amniotomy may be helpful in the transition from latent to active labor. Based on the same Cochrane review finding, improved satisfaction and lower cesarean and operative vaginal delivery rates, emotional support is recommended. The potential effect of epidural analgesia on duration of labor is noted as a potential consideration in allowing longer durations before intervention, but there are no recommendations about specific techniques. Cervical exam frequency, intrauterine pressure monitoring, oxytocin dosing protocols, methods for routine fetal monitoring, or timing of pushing in the second labor are not discussed, consistent with the relative paucity of evidence.

The impact of regional anesthesia on the length of the first stage of labor is uncertain, leading to conflicting recommendations from different professional societies. Our findings do not provide greater clarity.

Applicability

Table 72 summarizes the applicability scores across KQs. Note that applicability ratings were performed for the 83 primary included studies and not for the included systematic reviews.

Table 72. Potential issues with applicability of included studies[a]

Issues	KQ 1 N=9	KQ 2 N=6	KQ 3 N=42	KQ 4 N=19	KQ 5 N=0	KQ 6 N=0	KQ 7 N=7	KQ 8 N=0	KQ 9 N=3	Total N=83
Population (P)										
Study population demographics not representative of intended population	3	2	15	0	0	0	1	0	0	20
Narrow or unrepresentative severity/stage/comorbidity	0	0	0	0	0	0	0	0	0	0
Intervention (I)										
Intervention details not representative of current practice	0	1	4	1	0	0	0	0	0	6

Issues	KQ 1 N=9	KQ 2 N=6	KQ 3 N=42	KQ 4 N=19	KQ 5 N=0	KQ 6 N=0	KQ 7 N=7	KQ 8 N=0	KQ 9 N=3	Total N=83
Change in standard of care	0	0	1	0	0	0	0	0	0	1
Comparator (C)										
Comparator not representative of current practice	0	0	9	1	0	0	0	0	0	10
Outcomes (O)										
Timing of outcome assessment	0	0	0	0	0	0	0	0	0	0
Setting (S)										
Standards or access to care vary from US setting	0	1	32	2	0	0	3	0	1	38
Specialty population or level of care	0	0	0	0	0	0	0	0	0	0

[a] Numbers in cells represent the number of included studies that were identified as having potential issues related to the specific item. Columns represent numbers for each key question and then for all included studies.

Two broad issues relate to the overall applicability of the available evidence to clinical practice in the United States—one geographic and one temporal. Many of the RCTs meeting our criteria were performed outside of the United States. Aside from issues related to differences in study oversight or reporting, the populations of these studies may differ from U.S. women in labor in terms of health systems, patient preferences and expectations, provider perceptions of risk, availability of resources, and so on. This is particularly relevant to studies that directly compared management strategies based on explicit criteria for defining abnormal labor and studies that attempted to define a "normal" duration of labor (KQ 1). Particularly for studies where the primary outcome is cesarean delivery, factors that affect the threshold for performing cesarean—both the explicit "cutpoint" for duration of labor used and broader factors ranging from the relative safety of surgery versus vaginal delivery in low resource settings to cultural expectations to legal concerns—may affect the estimates of effectiveness of an intervention.

A number of studies included the use of a partogram—a graphical comparison of a woman's labor progress compared to a standard—with thresholds for intervention clearly identified. Strength of evidence was judged to be low, with one major factor being a lack of U.S.-based studies. In low-resource settings, the use of a partogram was associated with lower overall cesarean delivery rates compared with labor managed without a partogram, and earlier interventions were associated with lower cesarean delivery rates. In high-resource settings, the use of a partogram that included an assessment of latent phase duration, and which had a threshold for action at 3 hours compared to 4 hours, had higher cesarean delivery rates; but otherwise the use of a partogram compared with no partogram, or other time intervals for action lines, did not affect mode of delivery, duration of labor, indication for cesarean delivery, or complications including postpartum hemorrhage, maternal infection, or neonatal acidemia.

Outside of U.S.-based settings, populations, health systems, and management of both prenatal and intrapartum care are quite different—and the impact of these differences on both the relative effectiveness and the absolute difference in outcomes is likely substantial.

Even more fundamentally, use of a tool such as a partogram, or specific interventions such as amniotomy, requires evidence on "normal" labor in order to define requires evidence on "normal" labor in order to define appropriate thresholds for action. The studies we reviewed that attempted to define "normal" labor differed based on parity, the time period in which the studies were conducted, and, among nulliparous women, maternal age. Evidence from the Consortium on Safe Labor (CSL), representing the most recent available large-scale population data[16] suggest a longer duration of first stage of labor compared to earlier studies, including the National Collaborative Perinatal Project.[17] However, the most striking difference between these two studies was the proportion of women who received oxytocin augmentation (14.6% in the NCPP cohort from 1959 to 1966 compared with 45.9% in the CSL cohort from 2002 to 2008).

The CSL population that was used to generate new labor curves consists of women who had spontaneous onset of labor and a vaginal delivery, and thus the labor curves presented provide an estimate of "normal" labor that does not end in a cesarean delivery. Since such a large proportion of women received augmentation, these data do not provide insight into the range of rates of labor progression among women who do not receive augmentation, and cannot provide insight into the relative harms and benefits of augmentation, or the most appropriate thresholds for the timing or dosing of augmentation. The association between a longer duration of the first stage of labor and the greater use of oxytocin among women with a vaginal delivery is consistent with the possibility that greater use of oxytocin may avoid cesarean delivery, but not with observed secular trends in cesarean delivery rates. One would expect that any changes in the threshold for cesarean delivery caused by greater "patience" (allowing a longer duration) and/or "medical management" (greater use of oxytocin) would lead to decreases in cesarean delivery rates.

In summary, evidence suggests that the specific criteria used to define "normal" labor, or a specific threshold for intervention, may affect cesarean delivery rates but not other maternal or neonatal outcomes in some settings. Yet there is no available evidence for the United States. Among women in the United States with spontaneous onset of labor and vaginal delivery, labor progression is slower for women having their first baby compared to women with prior deliveries, but the high proportion of women receiving oxytocin augmentation prevents drawing any inferences about the "normal" labor curve in women with spontaneous onset of labor, no interventions to augment labor, and no adverse maternal or neonatal outcomes.

Implications for Clinical and Policy Decisionmaking

There is widespread consensus that the current cesarean delivery rate in the United States is too high, and national organizations suggest implementation of strategies to safely decrease the cesarean delivery rate. Cesarean delivery is performed for a range of indications, and any strategy to reduce the overall rate needs to be multifaceted and based on achieving an optimal rate (balancing both maternal and neonatal outcomes) for each indication—although the optimal cesarean delivery rate that balances maternal and neonatal outcomes is not known. Because abnormal labor is a common indication for cesarean delivery (particularly for first cesareans), strategies for reducing the rate of cesarean for prolonged labor have the potential to reduce the overall rate by decreasing both primary and repeat cesareans.

Data on the "normal" range of labor duration from the CSL are useful for developing guidance for when (or whether) to consider intervention with cesarean section. However,

because (a) a very high proportion of women received oxytocin augmentation and (b) separate curves are not reported for those with and without augmentation, this evidence is not helpful in developing strategies for when to initially intervene with oxytocin or other labor stimulus.

Given the evidence that partograms have been useful in other settings, and the potential benefit of formal decision tools seen in other conditions, there may be potential for incorporating more direct decision aids to help guide when, or when not, to intervene in otherwise uncomplicated labor based on the temporal progress of labor. Such tools need to incorporate both clinical evidence and patient preferences for choices about the process of labor.

Limitations of the Systematic Review Process

Several aspects of the review process may have affected the results. First, there were constraints in our search strategy, developed in consultation with the Key Informants and TEP. We limited the search to papers published after January 2005. This meant that studies completed prior to the cutoff date, which otherwise might have met inclusion criteria, were excluded. While we believe that the majority of these studies were included in the systematic reviews we used to supplement each KQ, it is possible that potentially relevant articles were missed. Given broad changes in clinical practice over the past decade, the impact of missing earlier studies on conclusions about comparative effectiveness of currently used treatment alternatives is unclear.

We also did not include studies published in languages other than English, primarily due to resource limitations. Given the high volume of literature available in English-language publications, the focus of our review on applicability to populations in the United States, and the scope of our current KQs, non-English articles were excluded.

Research Recommendations

We identified several areas of needed future research:

- It would be extremely useful to have separate labor curves derived from contemporary U.S. data for women with spontaneous onset of labor, no augmentation with oxytocin or other pharmacologic agents, and vaginal delivery of healthy baby, stratified by parity, as well as for women with augmented labor. Such labor curves would provide a better understanding of the modern natural course of labor and may provide better information on when to initiate agents to augment labor and when to proceed with cesarean delivery.
- Evaluation of specific labor management strategies (including the use of partograms) derived from contemporary data sources such as the CSL should be a priority. This evaluation should include comparison of different methods for integrating decision support into existing technologies, such as methods and timing of augmenting labor (oxytocin administration, artificial rupture of the membranes), fetal monitoring, tools to monitor uterine contraction strength and frequency, and the impact of supportive therapies (massage, fluids, nutrition, positioning) on mode of delivery. This evaluation would help generate best practice recommendations for safe reduction of the primary cesarean delivery rate while balancing maternal and neonatal outcomes.
- Given the importance of the labor process to patient preferences and their birthing experience and the lack of evidence about the impact of available interventions on these preferences, the development of tools for estimating patient preferences for both the process and maternal and neonatal outcomes of labor should be a priority. Discrete choice

experiments would be one method appropriate for estimating preferences for these complex tradeoffs.

- Comparison of patient preferences of nulliparous to multiparous women are of great interest as preferences may vary based on prior labor experiences and expectations.
- Studies of these tools/methods should also explore the complexity of decision making that needs incorporate both maternal and paternal preferences, as well as parental preferences as surrogate for infants. Validated measures should be incorporated into clinical trials and prospective studies as specific outcomes.

Conclusions

Dystocia is a common indication for cesarean delivery. Recent data demonstrate that the normal progress of labor with current practice is quite different from curves originally described, although there is still uncertainty about the duration of “normal” labor in the absence of augmentation. Amniotomy and oxytocin decrease duration of labor without increasing cesarean delivery. Emotional support reduces operative delivery rates and patient satisfaction. Further work is needed to identify strategies for management of labor that optimize maternal and neonatal outcomes and patient preferences while minimizing cesarean delivery rates.

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Acronyms and Abbreviations

AE	Adverse events
AHRQ	Agency for Healthcare Research and Quality
AMSTAR	Measurement tool to assess the methodological quality of systematic reviews
aOR	Adjusted odds ratio
AROM	Artificial rupture of membranes
BMI	Body mass index
CDSR	Cochrane Database of Systematic Reviews
CI	Confidence interval
CPAP	Continuous positive airway pressure;
CSE	Combined spinal epidural
CSL	Consortium on Safe Labor
EA	Epidural analgesia
EHC	Effective Health Care
FHR	Fetal heart rate
HOB	Head of bed
IQR	Interquartile range
KQ	Key Question
MA	Meta-analysis
MD	Mean difference
NA	Not applicable
NCPP	National Collaborative Perinatal Project
NICU	Neonatal intensive care unit
NR	Not reported
NS	Not significant
NRFHT	Nonreassuring Fetal Heart Rate Tracing
OR	Odds ratio
PCIA	Patient-controlled intravenous analgesia
PICOTS	Population, Intervention, Comparator, Outcomes, Timing, Setting
PSU	Prince of Songkla University
RCT	Randomized controlled trial
RR	Relative risk
SD	Standard deviation
SOE	Strength of evidence
SR	Systematic review
WMD	Weighted mean difference