

Evidence-based Practice Center Systematic Review Protocol

Project Title: Labor Dystocia

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Amendment Date(s) if applicable: July 12, 2016

(Amendments Details—see Section VII)

I. Background and Objectives for the Systematic Review

Approximately 80% of American women will eventually have at least one child,¹ and the majority of these women will undergo 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 labor³ to entrapment of the fetal shoulders after delivery of the head (“shoulder dystocia,” an obstetric emergency). Prolonged labor may increase the risk for maternal and neonatal infection, fetal distress, neonatal asphyxia, uterine rupture, and postpartum hemorrhage; it may also be a marker for an increased risk of maternal pelvic floor and genital trauma during delivery (with a subsequent increase risk for future incontinence and pelvic organ prolapse) and of shoulder dystocia. These increased risks are the underlying indication for cesarean delivery in the setting of labor dystocia. On the other hand, cesarean delivery 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. Furthermore, having one cesarean delivery increases the likelihood of having subsequent cesarean deliveries.³ A woman’s risk for abnormal placentation (placenta previa or accreta, which are each associated with significant maternal and neonatal morbidity as well as mortality) is directly related to the number of prior cesarean deliveries a woman has had.⁴ Methods to prevent a woman’s first, or primary caesarean delivery, may lead to significant improvements in maternal and neonatal outcomes.³

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,⁵ and 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 characteristics⁶ (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).

Although there is no consensus on the “optimal” cesarean section rate (conceptually, the rate which strikes a balance between harms and benefits 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.^{3,7} Because dystocia is a major indication for primary cesarean section, and because rates of vaginal birth after cesarean (VBAC) have been declining, safely reducing the rate of cesarean deliveries performed for labor dystocia

should substantially reduce the overall cesarean rate. For this reason, ACOG and the Society for Maternal-Fetal Medicine (SMFM) have issued a joint consensus statement aimed at “preventing the first cesarean delivery.”³ For the purposes of this protocol and the subsequent 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).

One source of uncertainty in the evidence is that the definitions for different phases of labor, and what constitutes “normal” labor, vary 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.⁸⁻¹⁰ The statistical approach used to define “normality”, primarily in reference to rates of cervical change, has also been the source of controversy.¹¹⁻¹³

Another source of uncertainty is that there are complex trade-offs 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).¹⁴⁻¹⁶ 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.¹⁶⁻¹⁸

II. The Key Questions

The draft key questions (KQs) developed during Topic Refinement were available for public comment from September 2, 2015, to September 22, 2015. The public comments focused on clarifying populations (primarily clarifying that women undergoing induction of labor, or who had experienced prior cesarean delivery, are excluded from this review), explicitly listing several setting comparisons (site of care or provider), expanding the outcomes to include neonatal length of stay, and clarifying the “reference” cervical examination frequency. There were also recommendations to consider a 2015 review that incorporates a range of clinical and non-clinical studies.¹⁹ The KQs were revised in response to all these comments, and we agreed to compare references from relevant sections of the above-mentioned review to those we identify using the search strategy and inclusion/exclusion criteria described below. Overall, the comments affirmed our planned approach. There were no other significant changes to the KQs or proposed methods.

The final KQs are:

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- vs. 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 vs 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?

PICOTS (population, interventions, comparators, outcomes, timing, and settings) for each KQ are listed below.

KQ 1:

- **Population:**

- Women aged 15-44 with uncomplicated pregnancy at 37-42 weeks gestation with a singleton pregnancy with vertex presentation and no prior history of cesarean delivery who have begun spontaneous labor (defined as the onset of spontaneous contractions—women who present with spontaneous rupture of membranes without contractions are not included in the review). 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. 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.

- **Interventions:**

- 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

- **Comparators:**

- Definitions of labor abnormalities based on older data (Friedman Curve)^{11,12}
- **Outcomes:**
 - 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 prolapse)
 - Maternal/paternal experience/satisfaction
 - 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 neonatal intensive care unit (NICU) > 24 hours
 - Neonatal length of stay
 - Process-related outcomes
 - Abnormal fetal heart rate tracing
 - Duration of labor
 - Mode of delivery (vaginal delivery, assisted vaginal delivery, cesarean delivery)
 - Parental preferences/satisfaction
- **Timing:**
 - Short-term: from beginning of spontaneous labor until discharge home (or equivalent for home delivery) for mother and infant
 - Long-term: from discharge onwards
- **Settings:**
 - Location: hospital, birthing center, home
 - Providers: obstetrician, family physician, nurse midwife, lay midwife, doula

KQ 2:

Source: www.effectivehealthcare.ahrq.gov

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- **Population:**
 - Same as for KQ 1
- **Interventions:**
 - Routine amniotomy (artificial rupture of membranes)
- **Comparators:**
 - No amniotomy, amniotomy for specific indications (e.g., placement of fetal scalp monitor or intrauterine pressure catheter)
- **Outcomes:**
 - Same as for KQ 1, plus umbilical cord prolapse
- **Timing:**
 - Same as for KQ 1
- **Settings:**
 - Same as for KQ 1

KQ 3:

- **Population:**
 - Same as for KQ 1
- **Interventions:**
 - Ambulation, routine maternal oxygen supplementation, specific nutritional recommendations or limitations, specific oral or parenteral hydration recommendations or limitations, continuous emotional support, peanut ball, Lamaze, hypnobirthing, hydrotherapy, positioning, acupuncture, other nonpharmacologic interventions identified through the search
- **Comparators:**
 - Usual care; interventions above compared to each other
- **Outcomes:**
 - Same as for KQ 1
- **Timing:**
 - Same as for KQ 1
- **Settings:**
 - Same as for KQ 1

KQ 4:

- **Population:**
 - Same as for KQ 1
- **Interventions:**
 - Epidural analgesia

- **Comparators:**
 - No analgesia, other methods of analgesia (e.g., parenteral narcotics such as morphine or nitrous oxide), nonpharmacologic methods of pain management
- **Outcomes:**
 - Same as for KQ 1
- **Timing:**
 - Same as for KQ 1
- **Settings:**
 - Same as for KQ 1

KQ 5:

- **Population:**
 - Same as for KQ 1
- **Interventions:**
 - Regular cervical examinations (timing may vary)
- **Comparators:**
 - Cervical examination only in the setting of clinical concern about labor progress; regular cervical examinations at differing frequencies
- **Outcomes:**
 - Same as for KQ 1
- **Timing:**
 - Same as for KQ 1
- **Settings:**
 - Same as for KQ 1

KQ 6:

- **Population:**
 - Women aged 15-44 with uncomplicated pregnancy at 37-42 weeks with suspected abnormalities of the first stage of labor
- **Interventions:**
 - Use of internal pressure catheters for measuring timing and strength of uterine contractions
- **Comparators:**
 - External tocodynamometry, no monitoring
- **Outcomes:**
 - Same as for KQ 1
- **Timing:**
 - Same as for KQ 1
- **Settings:**

- Same as for KQ 1

KQ 7:

- **Population:**
 - Women aged 15-44 with uncomplicated pregnancy at 37-42 weeks with a diagnosed abnormality of the first stage of labor
- **Interventions:**
 - Infusion of low-dose oxytocin
- **Comparators:**
 - High-dose oxytocin; nipple stimulation; maternal oxygen supplementation as an adjunct to oxytocin; different formulations of oxytocin
- **Outcomes:**
 - Same as for KQ 1
- **Timing:**
 - Same as for KQ 1
- **Settings:**
 - Same as for KQ 1

KQ 8:

- **Population:**
 - 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
- **Interventions:**
 - Electronic fetal monitoring (external or internal)
- **Comparators:**
 - Intermittent auscultation of fetal heart rate
- **Outcomes:**
 - Maternal
 - Same as for KQ1
 - Neonatal
 - Same as for KQ1
- **Timing:**
 - Same as for KQ 1
- **Settings:**
 - Same as for KQ 1

KQ 9:

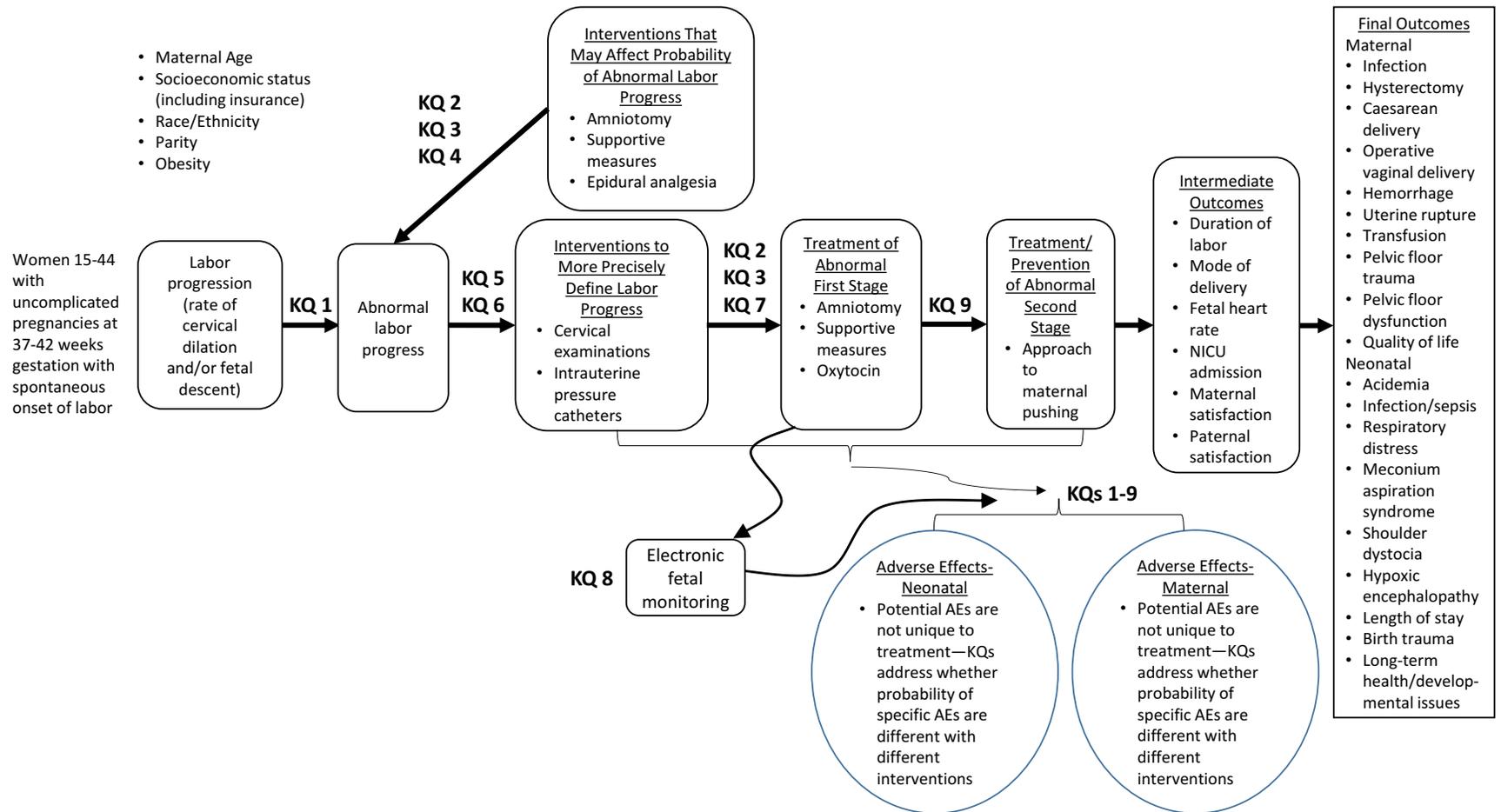
- **Population:**

- 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
- **Interventions:**
 - Immediate pushing upon complete dilation
- **Comparators:**
 - Other specified maternal techniques/approaches to pushing
- **Outcomes:**
 - Same as for KQ 1
- **Timing:**
 - Same as for KQ 1
- **Settings:**
 - Same as for KQ 1

III. Analytic Framework

The analytic framework presented in Figure 1 illustrates the population, interventions, outcomes, and adverse effects that will guide the literature search and synthesis. This figure 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



IV. Methods

In developing this comprehensive review, we will apply the rules of evidence and evaluation of strength of evidence recommended by the Agency for Healthcare Research and Quality (AHRQ) in its *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* (hereafter referred to as the Methods Guide).²⁰ We will follow the methodology guidance developed by the Evidence-based Practice Centers in the Methods Guide for literature search strategies, inclusion/exclusion of studies in our review, abstract screening, data abstraction and management, assessment of methodological quality of individual studies, data synthesis, and grading of evidence for each KQ.

We will seek the input of an external Technical Expert Panel (TEP) when warranted to aid in identifying the outcomes of critical importance for assessment. In addition to teleconference discussions, this input would be anticipated to take the form of formal surveys and numerical ranking.

Criteria for Inclusion/Exclusion of Studies in the Review

Table 1. Inclusion and exclusion criteria

PICOTS Element	Inclusion Criteria	Exclusion Criteria
Populations	<ul style="list-style-type: none"> • 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 • 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. 	<ul style="list-style-type: none"> • 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 • 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

PICOTS Element	Inclusion Criteria	Exclusion Criteria
Interventions	<ul style="list-style-type: none"> • 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 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	<ul style="list-style-type: none"> • KQ 1: Definitions of labor abnormalities based on older data (Friedman Curve)^{11,12} • 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	<ul style="list-style-type: none"> • KQs 1, 3-9: <ul style="list-style-type: none"> ○ Maternal 	For admission to NICU, studies which do not report length of stay if indication

Source: www.effectivehealthcare.ahrq.gov

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PICOTS Element	Inclusion Criteria	Exclusion Criteria
	<ul style="list-style-type: none"> • 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 prolapse) • Maternal/paternal experience/satisfaction ○ Neonatal <ul style="list-style-type: none"> • 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 ○ Process-related outcomes <ul style="list-style-type: none"> • Abnormal fetal heart rate tracing • Duration of labor • Mode of delivery (vaginal delivery, assisted vaginal delivery, cesarean delivery) • Parental preferences/satisfaction • KQ 2 : <ul style="list-style-type: none"> ○ Same as above plus umbilical cord prolapse 	distribution is not reported
Timing	<ul style="list-style-type: none"> • KQs 1-9: <ul style="list-style-type: none"> ○ Short-term: from beginning of spontaneous labor until discharge home (or equivalent for home delivery) for mother and infant ○ Long-term: from discharge onwards 	
Settings	<ul style="list-style-type: none"> • KQs 1-9: <ul style="list-style-type: none"> ○ Location: hospital, birthing center, home ○ Providers: obstetrician, family physician, nurse 	

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PICOTS Element	Inclusion Criteria	Exclusion Criteria
	midwife, lay midwife, doula	
Study design	<ul style="list-style-type: none"> • KQ 1: <ul style="list-style-type: none"> ○ Original data, including systematic reviews and meta-analyses ○ RCTs, prospective and retrospective observational studies with comparator ○ Observational studies: sample size ≥ 100 subjects • KQs 2-9: <ul style="list-style-type: none"> ○ Original data, including systematic reviews and meta-analyses ○ RCTs 	<ul style="list-style-type: none"> • Editorials, nonsystematic reviews, letters, case series, case reports, abstracts only • Because observational studies with fewer than 100 subjects are often underpowered, they will be excluded.
Publications	<ul style="list-style-type: none"> • KQs 1-9: <ul style="list-style-type: none"> ○ English-language only ○ Published January 1, 2005 to present ○ Relevant methods articles (used for background only) 	<ul style="list-style-type: none"> • 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 will be excluded.^a

^aIt is the opinion of the investigators that the resources required to translate non-English articles would not be justified by the low potential likelihood of identifying relevant data unavailable from English-language sources.

Abbreviations: CPAP = continuous positive airway pressure; KQ(s) = key question(s); NICU = neonatal intensive care unit; PICOTS = populations, interventions, comparators, outcomes, timing, settings; RCTs = randomized controlled trial

Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies to Answer the Key Questions

To identify relevant published literature, we will search PubMed[®], Embase[®], CINAHL[®], and the Cochrane Database of Systematic Reviews, limiting the search to studies published from January 1, 2005, to the present. These databases were selected based on internal expert opinion that they would identify most of the relevant literature on this topic, and reflects the databases used in related systematic reviews, particularly reviews conducted by the Cochrane Pregnancy and Childbirth Group.

Our proposed search strategy for PubMed is provided in Table 2; this strategy will be adapted as appropriate for searching the other databases. Where possible, we will use existing validated search filters (such as the Clinical Queries Filters in PubMed). An experienced search librarian will guide all searches. We will supplement the electronic searches with a manual search of citations from a set of key primary and review articles. The reference list for identified key articles will be manually hand-searched and cross-referenced against our database, and additional relevant manuscripts will be retrieved. All citations will be imported into an electronic bibliographical database (EndNote[®] Version X7; Thomson Reuters, Philadelphia, PA).

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Table 2. PubMed search strategy

Set #	Terms
#1	"Dystocia"[Mesh] OR "Dystocia"[tiab] OR "Dystocias"[tiab] OR "hypotonic contractions"[tiab] OR "slow progress"[tiab] OR "lack of progress"[tiab] OR "unsatisfactory progress"[tiab] OR "failure to progress"[tiab] OR "abnormal labor"[tiab] OR "labor arrest"[tiab] OR "labour arrest"[tiab] OR "arrested labor"[tiab] OR "arrest of labor"[tiab] OR "prolonged labor"[tiab] OR "dysfunctional labor"[tiab] OR "obstructed labor"[tiab] OR "labor obstruction"[tiab] OR "abnormal labour"[tiab] OR "labour arrest"[tiab] OR "arrested labour"[tiab] OR "arrest of labour"[tiab] OR "prolonged labour"[tiab] OR "dysfunctional labour"[tiab] OR "obstructed labour"[tiab] OR "labour obstruction"[tiab] OR "inefficient uterine contractions"[tiab] OR "protracted"[tiab] OR "arrested descent"[tiab] OR "arrest of descent"[tiab] OR "inertia uteri"[tiab] OR "uterine inertia"[tiab] OR "uterus inertia"[tiab] OR "Uterine Atony"[tiab] OR "inefficient uterine action"[tiab] OR "prolonged deceleration phase"[tiab] OR "abnormal progress"[tiab] OR "transverse arrest"[tiab] OR "prolonged second stage"[tiab] OR "delayed second stage"[tiab] OR "non-progressive labor"[tiab] OR "non-progressive labour"[tiab] OR "protraction disorder"[tiab] OR "protraction disorders"[tiab] OR "arrest disorder"[tiab] OR "arrest disorders"[tiab] OR "hypocontractile labour"[tiab] OR "hypocontractile labor"[tiab]
#2	"Labor, Obstetric"[Mesh] OR "Delivery, Obstetric"[Mesh] OR "Labor Onset"[Mesh] OR "Obstetric Delivery"[tiab] OR "Obstetric Deliveries"[tiab] OR "obstetric labor"[tiab] OR "obstetric labour"[tiab] OR "normal labor"[tiab] OR "normal labour" OR "term labor" OR "term labour" OR "labor onset"[tiab] OR "labour onset"[tiab] OR "Second Labor Stages"[tiab] OR "Second Labour Stages"[tiab] OR "Second Stage of Labor"[tiab] OR "Second Stage of Labour"[tiab] OR "Second Stage Labor"[tiab] OR "Second Stage Labour"[tiab] OR "First Stage of Labor"[tiab] OR "First Stage of Labour"[tiab] OR "First Stage Labor"[tiab] OR "First Stage Labour"[tiab] OR ((labour[tiab] OR labor[tiab]) AND ("Pregnancy"[Mesh:NoExp] OR "Pregnant Women"[Mesh] OR "pregnancy"[tiab] OR "pregnant"[tiab] OR "pregnancies"[tiab] OR "gestation"[tiab] OR "Prenatal Care"[Mesh] OR "childbirth"[tiab] OR "Parity"[Mesh] OR "nulliparous"[tiab] OR "multiparous"[tiab] OR "Cervical Dilatation"[tiab] OR "Cervical Dilatations"[tiab]))
#3	#1 AND #2
#4	("Labor Onset"[Mesh] OR "labor onset"[tiab] OR "labour onset"[tiab] OR "Second Labor Stages"[tiab] OR "Second Labour Stages"[tiab] OR "Second Stage of Labor"[tiab] OR "Second Stage of Labour"[tiab] OR "Second Stage Labor"[tiab] OR "Second Stage Labour"[tiab] OR "First Stage of Labor"[tiab] OR "First Stage of Labour"[tiab] OR "First Stage Labor"[tiab] OR "First Stage Labour"[tiab]) AND ("Time Factors"[Mesh] OR "Pregnancy Outcome"[Mesh])
#5	#3 OR #4
#6	#5 NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT (animals[mh] NOT humans[mh])
#7	Limits: English; Date-2005 - Present
#8	"Amnion/surgery"[Mesh] OR "Amniotomy"[tiab]
#9	"Exercise"[Mesh] OR "walking"[tiab] OR "ambulation"[tiab] OR "Nutrition Processes"[Mesh] OR "Eating"[tiab] OR "drinking"[tiab] OR "Diet"[Mesh:NoExp] OR "Fasting"[Mesh] OR "fasting"[tiab] OR "nutrition"[tiab] OR "intravenous dextrose"[tiab] OR "normal saline"[tiab] OR "Infusions, Intravenous"[Mesh] OR "Intravenous Drip"[tiab] OR "Infusion Drip"[tiab] OR "IV hydration"[tiab] OR "intravenous hydration"[tiab] OR "Ringer solution"[tiab] OR "Ringer-locke solution"[tiab] OR "hydration fluids"[tiab] OR "oral fluids"[tiab] OR "Bradley Method"[tiab] OR "Pain/prevention and control"[Mesh] OR "Douglas"[Mesh] OR "Douglas"[tiab] OR "Doula"[tiab] OR "labor coach"[tiab] OR "labor coaches"[tiab] OR "Natural Childbirth"[Mesh] OR "emotional support"[tiab] OR "Coaching"[tiab] OR "Peanut ball"[tiab] OR "birthing ball"[tiab] OR "childbirth education"[tiab] OR

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	"Lamaze"[tiab] OR "hypnobirthing"[tiab] OR "hypnosis"[tiab] OR "HypnoBabies"[tiab] OR "Complementary Therapies"[Mesh] OR "Healthy Birth"[tiab] OR "Patient Care Planning"[Mesh:NoExp] OR "supplemental oxygen"[tiab] OR "oxygen supplementation"[tiab] OR "Fetal Distress/therapy"[Mesh] OR "Oxygen Inhalation Therapy"[Mesh:NoExp] OR "Hydrotherapy"[Mesh] OR "hydrotherapy"[tiab] OR "hydrotherapies"[tiab] OR "Whirlpool Baths"[tiab] OR "Whirlpool Bath"[tiab] OR "birthing tub"[tiab] OR "Warm Baths"[tiab] OR "warm bath"[tiab] OR "Patient Positioning"[Mesh] OR "supine"[tiab] OR "Posture"[Mesh] OR "Psychoprophylaxis"[tiab] OR "Acupuncture"[tiab] OR "Acupressure"[tiab] OR "Aromatherapy"[tiab] OR "music therapy"[tiab] OR "massage"[tiab])
#10	"analgesia, epidural"[MeSH] OR "Anesthesia, Epidural"[Mesh] OR "epidural"[tiab]
#11	"Gynecological Examination"[Mesh] OR "Gynecological Examination"[tiab] OR "Gynecological Examinations"[tiab] OR "Gynecological Exam"[tiab] OR "Gynecological Exams"[tiab] OR "Gynaecological Examination"[tiab] OR "Gynaecological Examinations"[tiab] OR "Gynaecological Exam"[tiab] OR "Gynaecological Exams"[tiab] OR "Vaginal Examination"[tiab] OR "Vaginal Examinations"[tiab] OR "Vaginal Exam"[tiab] OR "Vaginal Exams"[tiab] OR "Cervical Examination"[tiab] OR "Cervical Examinations"[tiab] OR "Cervical Exam"[tiab] OR "Cervical Exams"[tiab] OR ("Cervix Uteri"[Mesh] AND ("Examination"[tiab] OR "Examinations"[tiab] OR "Exam"[tiab] OR "Exams"[tiab])) OR "Pelvic Examination"[tiab] OR "Pelvic Examinations"[tiab] OR "Pelvic Exam"[tiab] OR "Pelvic Exams"[tiab]
#12	"Uterine Monitoring"[Mesh] OR "Uterine Monitoring"[tiab] OR "intrauterine pressure catheter"[tiab] OR "intrauterine pressure catheters"[tiab] OR "IUPC"[tiab] OR Tocodynamometry[tiab] OR Tocography[tiab] OR Tocograms[tiab] OR Tocogram[tiab]
#13	"Oxytocin"[Mesh] OR "Oxytocics"[Mesh] OR "Ocytocin"[tiab] OR "Syntocinon"[tiab] OR "Pitocin"[tiab] OR "nipple stimulation"[tiab]
#14	"Valsalva Maneuver"[Mesh] OR "Valsalva Maneuvers"[tiab] OR "Valsalva Maneuver"[tiab] OR "Valsalva pushing"[tiab] OR "passive descent"[tiab] OR "delayed pushing"[tiab] OR "open glottis pushing"[tiab]
#15	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR systematic[sb] OR "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[tiab] OR "meta-analyses"[tiab]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT (animals[mh] NOT humans[mh])
#16	(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)
#17	#2 AND #15 AND #16
#18	Limits: English; Date-2005 - Present
#19	#7 OR #18

As a mechanism to ascertain publication bias in recent studies, we will search ClinicalTrials.gov to identify completed but unpublished studies (we will also explore the possibility of publication bias specifically in our quantitative synthesis of the included literature through meta-analysis techniques). 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.

We will use several approaches to identifying relevant gray literature, including notification to stakeholders (including drug and device manufacturers) of requests to submit scientific information packets and a search of U.S. Food and Drug Administration

(FDA) device registration studies and new drug applications. We will also search study registries for relevant articles from completed studies. Gray literature databases will include ClinicalTrials.gov, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal, and the National Guidelines Clearinghouse.

For citations retrieved from PubMed, Embase, CINAHL, and the Cochrane Database of Systematic Reviews, two reviewers using prespecified inclusion/exclusion criteria will review titles and abstracts for potential relevance to the research questions. Inclusion at the title screening level will be liberal; if a single reviewer believes an article may contain relevant information based on title, the article will move to the next level (abstract) for further screening. Articles included by either reviewer will undergo full-text screening. At the full-text screening stage, two independent reviewers must agree on a final inclusion/exclusion decision. Disagreements that cannot be resolved by the two reviewers will be resolved by a third expert member of the team. Articles meeting eligibility criteria (see Table 1) will be included for data abstraction. At random intervals during screening, quality checks by senior team members will occur to ensure that screening and abstraction is consistent with inclusion/exclusion criteria and abstraction guidelines. We will make screening decisions and abstract data based on the published literature and available online appendices. We will not contact study authors for additional data. All results will be tracked using the DistillerSR data synthesis software program (Evidence Partners Inc., Manotick, ON, Canada).

Data Abstraction and Data Management

The research team will create data abstraction forms for the KQs that will be programmed in the DistillerSR software. Based on their clinical and methodological expertise, a pair of researchers will be assigned to abstract data from each of the eligible articles. One researcher will abstract the data, and the second will over-read the article and the accompanying abstraction to check for accuracy and completeness. Disagreements will be resolved by consensus or by obtaining a third reviewer's opinion if consensus cannot be reached. We will link studies to avoid duplication of patient cohorts. Guidance documents will be drafted and provided to the researchers to aid both reproducibility and standardization of data collection.

We will design the data abstraction forms for this project 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 will pay 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, BMI, parity), and study design (e.g., RCT versus observational) that may be related to outcomes. In addition, we will describe comparators carefully, as treatment standards may have changed during the period covered by the review. The safety outcomes will be framed to help identify adverse events, including those from drug therapies and those resulting from misdiagnosis and labeling. Data necessary for assessing quality and applicability, as described in the Methods Guide,²⁰ will also be abstracted. Before they are used, abstraction form templates will be pilot-

tested with a sample of included articles to ensure that all relevant data elements are captured and that there is consistency and reproducibility between abstractors. Forms will be revised as necessary before full abstraction of all included articles. Final abstracted data will be uploaded to SRDR per EPC requirements.

Assessment of Methodological Risk of Bias of Individual Studies

During abstraction, we will assess methodological quality, or risk of bias, for each individual study based on the Cochrane Risk of Bias²¹ tool for randomized studies, and the Newcastle-Ottawa Scale²² for observational studies. We will supplement these tools with additional assessment questions, such as use of appropriate analysis, based on recommendations in the AHRQ's Methods Guide.²⁰ Briefly, we will rate each study as being of good, fair, or poor quality based on its adherence to well-accepted standard methodologies. Disagreements will be resolved as described above, either by consensus or by obtaining a third reviewer's opinion if consensus cannot be reached. For all studies, the overall study quality will be assessed as follows:

- 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. 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 will be outcome-specific such that a given study that analyzes its primary outcome well but did an incomplete analysis of a secondary outcome would be assigned a different quality grade for each of the two outcomes. Studies of different designs will be graded within the context of their respective designs. Thus, RCTs will be graded good, fair, or poor, and observational studies will separately be graded good, fair, or poor.

Data Synthesis

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

One potentially important consideration is the effect of changing diagnostic thresholds on estimates of comparative effectiveness in terms of both benefits and harms. It is possible that more conservative definitions of labor dystocia based on more recent evidence would substantially change the probability of an adverse outcome because of differences in sensitivity and specificity compared to older criteria, which would have the effect of changing both the expected probability of events and the absolute number of events. This in turn could have substantial impact on the precision of effect estimates, as well as on estimates of the absolute effect (including number needed to treat or harm). We will carefully assess the implications of this using the available evidence through simple modeling, and discuss any necessary amendments to the protocol with AHRQ and the TEP.

We will then determine 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, conceptual homogeneity of the studies, completeness of the reporting of results, and the adequacy and completeness of any existing meta-analyses. Because there are a large number of existing systematic reviews for this topic, particularly from the Cochrane Collaboration, we will consider these results using suggested guidance from the Methods Guide chapter on integrated bodies of evidence,²³ as outlined in more detail below. As recommended by the Methods Guide, judgments about the benefit of performing a new quantitative estimate will be based 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 is appropriate, we will use random-effects models to synthesize the available evidence quantitatively. We will test 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 will also perform fixed-effect meta-analyses. We will present summary estimates, standard errors, and confidence intervals. We anticipate that intervention effects may be heterogeneous. We hypothesize that the methodological quality of individual studies, study type, the characteristics of the comparator, and patients' underlying clinical presentation will be associated with the intervention effects. If there are sufficient studies, we will perform subgroup analyses and/or meta-regression analyses to examine these hypotheses. We will perform quantitative and qualitative syntheses separately by study type and discuss their consistency qualitatively.

For a decision analysis or simulation model, feasibility will be based on a judgment about the degree to which such an analysis will provide additional insight into the KQs based on the available evidence—for example, a stochastic simulation of the likelihoods of caesarian delivery based on two different criteria for diagnosis of abnormal labor based on distributions of labor progression in a large population would give insight into the existing degree of certainty about the benefit-harm trade-off associated with each protocol, which would inform future research prioritization.²⁴ If a model is used, we will

follow suggested guidance on the use of simulation models in EPC reports as developed by the Brown EPC.²⁵

Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes

We will grade 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 will be assessed using the approach described in AHRQ's Methods Guide.^{20,26} 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 in detail above. Additional domains to be used when appropriate (most relevant to observational studies) are dose-response association, impact of plausible residual confounders, and strength of association (magnitude of effect). When the body of evidence for a particular outcome includes both RCTs and observational studies, we will grade each study type separately using design-specific criteria. In considering the overall strength of the entire body of evidence, we will consider the extent to which the observational evidence is consistent with RCT data, particularly with regard to direction and magnitude of effect. Because of the risk of unmeasured confounding, observational studies would generally not contribute to estimates of the magnitude of effect, and judgment 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.²⁷ These domains will be considered qualitatively, and a summary rating of high, moderate, or low strength of evidence will be assigned for each outcome after discussion by two reviewers. In some cases, high, moderate, or low ratings will be impossible or imprudent to make, for example, when no evidence is available or when evidence on the outcome is too weak, sparse, or inconsistent to permit any conclusion to be drawn. In these situations, a grade of "insufficient" will be assigned. This four-level rating scale consists 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 systematic reviews, some with meta-analyses, in this area. We will use the recommendations outlined in the Methods Guide chapter on integrating existing systematic reviews in incorporating this body of evidence into our review. Briefly, we will confirm that a given paper is a systematic review 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 will be assessed based on comparability of PICOTS and the extent to which included studies reflect current practice. The quality of relevant existing reviews will be graded using a components approach, with key components including 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. If the risk of bias assessments from the existing review are compatible with our component based approach, we will use these assessments where feasible after reviewing a sample of studies to confirm concordance with our approach—in the event the approaches are not concordant, we will perform an independent synthesis of all studies meeting our specified inclusion criteria. Key aspects of previous reviews to be described include number and types of studies included, strength of evidence assessment, and overall qualitative or quantitative findings. Newly identified studies will be presented separately from the results of existing reviews. Overall strength of evidence findings will be based on the body of evidence based on the primary evidence, not the quality or number of existing reviews.

Assessing Applicability

We will assess applicability across our key questions using the method described in AHRQ's Methods Guide.^{20,28} 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 are different across studies that recruit different populations (e.g., age groups, ADHD presentations, exclusions for comorbidities) or use 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 will use a checklist to guide the assessment of applicability. We will use these data 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 will summarize issues of applicability qualitatively.

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VI. Definition of Terms

ADHD	Attention deficit hyperactivity disorder
AHRQ	Agency for Healthcare Research and Quality
BMI	Body mass index
CPAP	Continuous positive airway pressure
FDA	Food and Drug Administration
ICTRP	International Clinical Trials Registry Platform
NICU	Neonatal intensive care unit
EPC	Evidence-based Practice Center
KQ(s)	Key question(s)

PICOTS	Population, interventions, comparators, outcomes, timing, settings
RCT(s)	Randomized controlled trial(s)
TEP	Technical Expert Panel
TOO	Task Order Officer
WHO	World Health Organization

VII. Summary of Protocol Amendments

Changes made to the protocol are summarized in the table below. Changes are not incorporated into the protocol body.

Table 3. Summary of Amendment Changes

Date	Section	Original Protocol	Revised Protocol	Rationale
7/6/2016	Section IV. Methods, Table 1. Inclusion and exclusion criteria - Population	The original protocol inclusion/exclusion criteria for Population listed the following exclusion reason as applicable to all KQs: 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	Clarified that this exclusion reason is only applicable to KQs 6-8	The Populations specified for KQs 1-5 and KQ 9 may be undergoing normal labor progression, thus this requirement is not applicable for all KQs.
7/6/2016	Section IV. Methods, Table 1. Inclusion and exclusion criteria – Study Design	NA	Specification added that retracted/ withdrawn articles will be excluded	Clarification of excluded article type
7/6/2016	Section IV. Methods, Table 1. Inclusion and exclusion criteria – Study Design	NA	Specification added that systematic reviews and meta-analyses will be excluded if they do not provide a quantitative summary of results for an outcome of interest	Clarification of inclusion/ exclusion requirements for systematic reviews and meta-analyses

Source: www.effectivehealthcare.ahrq.gov

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7/6/2016	Section IV. Methods, Searching the Evidence	Original protocol anticipated a search of FDA device registration studies and new drug applications (NDAs) as part of the gray literature assessment	Search of this source no longer proposed; gray literature assessment will include ClinicalTrials.gov, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal, and the National Guidelines Clearinghouse.	In the opinion of the investigators, the FDA source was determined unlikely to provide additional impactful data beyond that available in the literature to be searched.
7/6/2016	Section IV. Methods, Risk of Bias	Original protocol anticipated use of the Cochrane Risk of Bias tool for randomized studies and the Newcastle-Ottawa Scale for nonrandomized studies	Quality assessments for randomized and nonrandomized study designs will be performed using design-specific criteria as described in the AHRQ Methods Guide.	The approach has been modified in order to apply the design-specific criteria outlined in the Methods Guide to both categories of study design.
7/6/2016	Section IV. Methods, Data	Original protocol mentioned misdiagnosis and labeling.	Text removed	This text was previously included in error.
7/6/2016	Section IV. Methods, Assessing Applicability	This section included ADHD presentation as part of a list of potential population differences among studies.	Removed ADHD presentation	This item was previously listed in error.

VIII. Review of Key Questions

AHRQ posted the key questions on the Effective Health Care Website for public comment. The EPC refined and finalized the key questions after review of the public comments, and input from Key Informants and the Technical Expert Panel (TEP). This input is intended to ensure that the key questions are specific and relevant.

IX. Key Informants

Key Informants are the end users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Within the EPC program, the Key Informant role is to provide input into identifying the Key Questions for research that will inform healthcare decisions. The EPC solicits input from Key Informants when developing questions for systematic review or when identifying high priority research gaps and needed new research. Key Informants are not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

Key Informants must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

X. Technical Experts

Technical Experts constitute a multi-disciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes and identify particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicting opinions are common and perceived as health scientific discourse that results in a thoughtful, relevant systematic review. Therefore study questions, design, and methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and recommend approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind nor do they contribute to the writing of the report. They have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

Technical Experts must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparation of the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers. The EPC will complete a disposition of all peer review comments. The disposition of comments for systematic reviews and technical briefs will be published three months after the publication of the evidence report.

Potential Peer Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than \$10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

XII. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than \$1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than \$1,000 will usually disqualify EPC core team investigators.

XIII. Role of the Funder

This project was funded under Contract No. HHS A290201500004I from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The Task Order Officer reviewed contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.