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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Cervical Ripening in the Outpatient Setting

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on *Cervical Ripening in the Outpatient Setting,* which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before 30 days after date of publication in the Federal Register.

ADDRESSES:

E-mail submissions: epc@ahrq.hhs.gov

Print submissions:

Mailing Address:

Center for Evidence and Practice Improvement

Agency for Healthcare Research and Quality

ATTN: EPC SEADs Coordinator

5600 Fishers Lane

Mail Stop 06E53A

Rockville, MD 20857
Shipping Address (FedEx, UPS, etc.):
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality
ATTN: EPC SEADs Coordinator
5600 Fishers Lane
Mail Stop 06E77D
Rockville, MD 20857

FOR FURTHER INFORMATION CONTACT:

Jenae Benns, Telephone: 301-427-1496 or Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION:

The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for Cervical Ripening in the Outpatient Setting. AHRQ is conducting this systematic review pursuant to Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a).

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Cervical Ripening in the Outpatient Setting*, including those that describe adverse events. The entire research protocol is available online at: https://effectivehealthcare.ahrq.gov/products/cervical-ripening/protocol

This is to notify the public that the EPC Program would find the following information on *Cervical Ripening in the Outpatient Setting* helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.

- *For completed studies that do not have results on ClinicalTrials.gov*, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.

- *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/email-updates.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

Key Questions (KQ)

KQ1: How do the effectiveness and harms of cervical ripening (CR) using prostaglandins compare in the outpatient vs. inpatient setting?

- 1a: How do effectiveness and harms vary by choice of prostaglandin?
- 1b: Do effectiveness and harms vary by important patient characteristics (such as gestational age, parity, uncomplicated pregnancy, prior cesarean delivery, etc.)?

KQ2: How do the effectiveness and harms of CR using mechanical methods (e.g., balloon catheters) compare in the outpatient vs. inpatient setting?

- 2a: How do effectiveness and harms vary by choice of mechanical method in the inpatient versus the outpatient setting?
- 2b: Do effectiveness and harms vary by important patient characteristics (such as gestational age, parity, uncomplicated pregnancy, prior cesarean delivery, etc.)?

KQ3: How do the effectiveness and harms of CR in the *outpatient setting* vary by method of CR compared with each other?

- 3a: Do effectiveness and harms vary by important patient characteristics (such as gestational age, parity, uncomplicated pregnancy, prior cesarean delivery, etc.)?

KQ4: How do the effectiveness and harms of different methods and protocols for fetal surveillance compare with each other or with no monitoring in pregnant women undergoing CR with prostaglandins?

- 4a. Do effectiveness and harms vary by important patient characteristics (such as gestational age, parity, uncomplicated pregnancy, prior cesarean delivery, etc.)?

Contextual Question: What evidence informs preference for or tolerability of different methods of CR in the outpatient setting or outpatient compared to the inpatient setting?

PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, Settings)

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs Outpatient	Inclusion Key Question 3: Outpatient comparison of methods	Inclusio Key Question Surveilla
Population	• Pregnant women ≥37 weeks undergoing CR in the outpatient setting • Important maternal subgroups: parity, maternal age, GBS status, diabetes (pre-gestational, gestational), hypertension (chronic, preeclampsia without severe features, gestational) • Important fetal subgroups: fetal growth restriction, gestational age (<39 weeks, 39 to 41 weeks, >41 weeks)	• Pregnant women ≥37 weeks undergoing CR in the outpatient setting • Important maternal subgroups: parity, maternal age, GBS status, diabetes (pre-gestational, gestational), hypertension (chronic, preeclampsia without severe features, gestational) • Important fetal subgroups: fetal growth restriction, gestational age (<39 weeks, 39 to 41 weeks, >41 weeks)	• Pregnant women ≥37 weeks undergoing CR in the outpatient setting • Important maternal subgroups: parity, maternal age, GBS status, diabetes (pre-gestational, gestational), hypertension (chronic, preeclampsia without severe features, gestational) • Important fetal subgroups: fetal growth restriction, gestational age (<39 weeks, 39 to 41 weeks, >41 weeks)	• Pregnant wor weeks underg with a prostag • Important ma subgroups: p maternal age status, diabet gestational, gestational), hypertension preeclampsia severe featur gestational) • Important feta subgroups: fe restriction, ge age (<39 wee 41 weeks, >4
Intervention	• Pharmacologic agents (prostaglandins) given in outpatient setting	• Mechanical methods (balloon catheters, laminaria tents) used in outpatient setting	Mechanical methods (balloon catheters, laminaria tents) or pharmacologic agents (prostaglandins)	• Any method c surveillance
Comparator	• Mechanical (i.e., balloon catheters, luminaria tents) and/or pharmacologic (i.e., prostaglandins) methods in the inpatient setting	• Mechanical (i.e., balloon catheters, luminaria tents) and/or pharmacologic (i.e., prostaglandins) methods in the inpatient setting	• Any comparator including alternative mechanical device or protocol, alternative pharmacologic agent or dose, combination mechanical and pharmacologic, placebo, and other CR methods excluded as intervention (e.g., Castor oil, acupuncture)	• Another meth surveillance • Another proto fetal surveillar the same me • No monitoring

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs Outpatient	Inclusion Key Question 3: Outpatient comparison of methods	Inclusio Key Question Surveilla
Outcomes Effectiveness (birth-related)	• **Total time admission to vaginal delivery; total L&D length of stay[c]** • **Cesarean delivery rate overall[c]** • Vaginal delivery within 24 hours • Failed induction rate, defined as: ○ CD in patient at <6cm dilation excluding fetal distress (labor dystocia, failure to progress, etc.) ○ CD in patient at <6 cm dilation for fetal distress • Cervical assessment at time of admission (e.g., latent vs. active phase, Bishop score, cervical dilation) • Time from ROM to delivery	• **Total time admission to vaginal delivery; total L&D length of stay[c]** • **Cesarean delivery rate overall[c]** • Vaginal delivery within 24 hours • Failed induction rate, defined as: ○ CD in patient at <6cm dilation excluding fetal distress (labor dystocia, failure to progress, etc.) ○ CD in patient at <6 cm dilation for fetal distress • Cervical assessment at time of admission (e.g., latent vs. active phase, Bishop score, cervical dilation) • Time from ROM to delivery	• **Total time admission to vaginal delivery; total L&D length of stay[c]** • **Cesarean delivery rate overall[c]** • Vaginal delivery within 24 hours • Failed induction rate, defined as: ○ CD in patient at <6cm dilation excluding fetal distress (labor dystocia, failure to progress, etc.) ○ CD in patient at <6 cm dilation for fetal distress • Cervical assessment at time of admission (e.g., latent vs. active phase, Bishop score, cervical dilation) • Time from ROM to delivery • Breastfeeding[b] • Maternal mood[b] • Mother-baby attachment[b]	• **Total time a to vaginal de total L&D le stay[c]** • **Cesarean de rate overall[c]** • Vaginal delive 24 hours • Failed inducti defined as: ○ CD in pati <6cm dilat excluding distress (l dystocia, f progress, ○ CD in pati cm dilation distress • Cervical asse time of admis latent vs. acti Bishop score dilation) • Time from R delivery

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs Outpatient	Inclusion Key Question 3: Outpatient comparison of methods	Inclusio Key Question Surveilla
Outcomes Fetal Harms	• **Perinatal Mortality**[c] • **Hypoxic-ischemic**[c] **encephalopathy**[c] • **Seizure**[c] • **Infection** (confirmed sepsis or pneumonia)[c] • **Meconium aspiration syndrome**[c] • **Birth trauma** (e.g., bone fracture, neurologic injury, or retinal hemorrhage)[c] • **Intracranial or subgaleal hemorrhage**[c] • Need for respiratory support within 72 hours after birth • Apgar score ≤3 at 5 minutes[a] • Hypotension requiring vasopressor support • Umbilical cord gas < pH 7.0 or 7.10	• **Perinatal Mortality**[c] • **Hypoxic-ischemic encephalopathy**[c] • **Seizure**[c] • **Infection** (confirmed sepsis or pneumonia)[c] • **Meconium aspiration syndrome**[c] • **Birth trauma** (e.g., bone fracture, neurologic injury, or retinal hemorrhage)[c] • **Intracranial or subgaleal hemorrhage**[c] • Need for respiratory support within 72 hours after birth • Apgar score ≤3 at 5 minutes[a] • Hypotension requiring vasopressor support • Umbilical cord gas < pH 7.0 or 7.10	• **Perinatal Mortality**[c] • **Hypoxic-ischemic encephalopathy**[c] • **Seizure**[c] • **Infection** (confirmed sepsis or pneumonia)[c] • **Meconium aspiration syndrome**[c] • **Birth trauma** (e.g., bone fracture, neurologic injury, or retinal hemorrhage)[c] • **Intracranial or subgaleal hemorrhage**[c] • Need for respiratory support within 72 hours after birth • Apgar score ≤3 at 5 minutes[a] • Hypotension requiring vasopressor support • Umbilical cord gas < pH 7.0 or 7.10	• **Perinatal Mo** • **Hypoxic-isch encephalopa** • **Seizure**[c] • **Infection** (co sepsis or pne • **Meconium a syndrome**[c] • **Birth trauma** bone fracture neurologic inj retinal hemorr • **Intracranial (subgaleal hemorrhage** • Need for resp support withir after birth • Apgar score : minutes[a] • Hypotension vasopressor : • Umbilical corc 7.0 or 7.10
Outcomes Maternal Harms	• **Hemorrhage requiring transfusion**[c] • **Postpartum hemorrhage by mode** (vaginal, cesarean)[c] • **Uterine infection** (i.e., choriamnionitis, administration of antibiotics in labor other than GBS prophylaxis)[c] • Placental abruption Uterine rupture • Umbilical cord prolapse • Duration of time between hospital admission to birth that is insufficient to enable complete GBS prophylaxis antibiotics administration per CDC guidelines	• **Hemorrhage requiring transfusion**[c] • **Postpartum hemorrhage by mode** (vaginal, cesarean)[c] • **Uterine infection** (i.e., choriamnionitis, administration of antibiotics in labor other than GBS prophylaxis)[c] • Placental abruption • Uterine rupture • Umbilical cord prolapse • Duration of time between hospital admission to birth that is insufficient to enable complete GBS prophylaxis antibiotics administration per CDC guidelines	• **Hemorrhage requiring transfusion**[c] • **Postpartum hemorrhage by mode** (vaginal, cesarean)[c] • **Uterine infection** (i.e., choriamnionitis, administration of antibiotics in labor other than GBS prophylaxis)[c] • Placental abruption Uterine rupture • Umbilical cord prolapse • Duration of time between hospital admission to birth that is insufficient to enable complete GBS prophylaxis antibiotics administration per CDC guidelines	• **Hemorrhage transfusion**[c] • **Postpartum hemorrhage** (vaginal, cesa • **Uterine infec** choriamnionit administration antibiotics in than GBS pro • Placental abr • Uterine ruptur • Umbilical corc • Duration of ti between hosp admission to is insufficient complete GB prophylaxis a administration guidelines

PICOTS	Inclusion Key Question 1: Prostaglandin Inpatient vs. Outpatient	Inclusion Key Question 2: Mechanical Method Inpatient vs Outpatient	Inclusion Key Question 3: Outpatient comparison of methods	Inclusio Key Question Surveilla
Timing	Maternal outcomes • From CR initiation to within 1-week following delivery Infant outcomes • Immediately following delivery	Maternal outcomes • From CR initiation to within 1-week following delivery Infant outcomes • Immediately following delivery.	Maternal and additional outcomes (i.e., breastfeeding, maternal mood, mother-baby attachment) • From CR initiation to 1-year postpartum Infant outcomes • Immediately following delivery	Maternal outcome • From CR initi within 1-week delivery Infant outcomes • Immediately delivery
Setting	• Inpatient versus outpatient settings	• Inpatient versus outpatient settings	• Outpatient setting	• Inpatient and settings
Study design	• Randomized Controlled Trials; recent high quality Systematic Reviews; if RCT evidence for benefits is insufficient, include large, high quality cohort studies comparing inpatient and outpatient setting. • Include high quality cohort and case-control studies for harms.	• Randomized Controlled Trials; recent high quality Systematic Reviews; if RCT evidence for benefits is insufficient, include large, high quality cohort studies comparing inpatient and outpatient setting. • Include high quality cohort and case-control studies for harms.	• Randomized Controlled Trials; recent high quality Systematic Reviews; if RCT evidence for benefits is insufficient, include large, high quality cohort studies comparing inpatient and outpatient setting. • Include high quality cohort and case-control studies for harms.	• Randomized Trials; recent quality Syste Reviews; if R evidence for insufficient, in large, high qu cohort studie comparing inp and outpatien • Include high cohort and ca studies for ha

[c] **(Bolded) items indicate Primary Outcomes**

CR = cervical ripening; CD = cesarean delivery; KQ = Key Question; ROM = rupture of membrane; CDC = Centers for Disease Control and Prevention; L&D = labor and delivery; RCTs = randomized controlled trials

Dated: 29 January 2020.

Virginia L. Mackay-Smith,

Associate Director,

Office of the Director, AHRQ.

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