Effective Health Care

Induction of Labor

Results of Topic Selection Process & Next Steps

The nominator, the American College of Obstetrics and Gynecology (ACOG), is interested in using a new systematic review on the benefits and harms of various methods for managing induction of labor to inform a clinical practice guideline. Due to limited program resources, the program will not develop a review at this time. No further activity on this topic will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Name: Induction of Labor

Topic #: 0651

Nomination Date: 08/06/2015

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Authors:
Christel Villarivera
Kara Winchell
Karli Kondo

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

Summary of Key Findings:

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review on this topic would not be duplicative of an existing product.
    - Although we found systematic reviews relevant to all key questions except 1b (methods for inducing labor for women with ruptured membranes) and 3 (fetal surveillance after prostaglandins), there was inconsistency in some of the findings, and there exists no comprehensive review. Our search resulted in 25 completed (14 of which are Cochrane reviews) and 3 in-process evidence reviews meeting inclusion criteria.
- Impact: An AHRQ product on this topic would have moderate impact potential. The standard of care is unclear, and a new review could address knowledge gaps identified in prior systematic reviews. This could influence practice and potentially improve health outcomes, including success of induction of labor.
- Feasibility: A new evidence review on induction of labor is feasible at this time.
    - While published literature is lacking for key questions 1c (methods for inducing labor for women with intrauterine fetal demise in the late second or third trimester), 3 (fetal surveillance after prostaglandins), and 4 (dosage and precautions after oxytocin for induced labor), a new AHRQ evidence review is feasible. Our search of PubMed resulted in 50 published studies meeting

inclusion criteria. We also identified 15 clinical trials relevant to the key " questions.

- Value: The potential for value is high, given that ACOG will use a new AHRQ evidence review to inform a clinical practice guideline.

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Introduction

Induction of labor is artificially starting labor near a pregnant woman's due date before it begins on its own. According to a recent report by the Centers for Disease Control and Prevention (CDC), after nearly 20 years of consecutive increases (9.6% in 1990 to 23.8% in 2010), the prevalence of induction of labor for singleton births has plateaued and is possibly seeing mild decrease with rates of 2011 (23.7%) and 2012 (23.3%).[1]

Induction of labor can occur because of medical or obstetrical indications such as preeclampsia, postdates (going past the due date), premature rupture of membranes, neonatal indications, etc. Over recent years there has been increasing concern about induction for non-medically indicated reasons (e.g. maternal request) and in inducing prior to 39 weeks gestational age.[2]

Induction often occurs in two stages, cervical ripening where the cervix is softened and begins dilation, and stimulation of labor. Physical and pharmacological methods are used for this process. Recently there is interest in what, if any, parts of the process might be safe to do as an outpatient. Decision-making involves a complex process of balancing maternal and neonatal risks.

Topic nomination 0651 was received on August 6, 2015. It was nominated by the American College of Obstetrics and Gynecology (ACOG). The questions for this nomination are:

Key Question 1. What is the effectiveness of available methods for labor induction

a. For women with no other co-occurring complicating conditions?
b. For women with ruptured membranes?
c. For women with intrauterine fetal demise in the late second or third trimester?

Key Question 2. What is the effectiveness of available methods for cervical ripening, including in an outpatient setting?

a. What are the most effective methods and dosage for administering prostaglandins?
b. What is the effectiveness of mechanical or other methods of cervical ripening?

Key Question 3. In pregnant women, what are the most effective methods for fetal surveillance after prostaglandin use?

Key Question 4. In pregnant women given oxytocin for induced labor, what is the most effective dosage and what precautions should be taken?

To define the inclusion criteria for the key questions we specify the population, interventions, comparators, outcomes, and setting (PICOS) of interest. See Table 1.

Table 1. Key Questions and PICOS "

Key Questions	1. What is the effectiveness of available methods for labor induction a. For women with no other co-occurring complicating conditions? b. For women with ruptured membranes? c. For women with intrauterine fetal demise in the late second or third trimester?	2. What is the effectiveness of available methods for cervical ripening, including in an outpatient setting? a. What are the most effective methods and dosage for administering prostaglandins? b. What is the effectiveness of mechanical or other methods of cervical ripening?	3. In pregnant women, what are the most effective methods for fetal surveillance after prostaglandin use?	4. In pregnant women given oxytocin for induced labor, what is the most effective dosage and what precautions should be taken?
Population	Pregnant women (with or without ruptured membranes or intrauterine fetal demise in the late second or third trimester) with indication for induction of labor	Pregnant women with an indication for cervical ripening	Pregnant women receiving prostaglandins	Pregnant women induced using oxytocin
Interventions	Methods of induction of labor	Methods of cervical ripening, including prostaglandins, mechanical and other methods	One method for fetal surveillance after prostaglandin administration	One dose of oxytocin
Comparators	Other methods of induction of labor	Other methods of cervical ripening; cervical ripening methods	Another method for fetal surveillance	Another dose of oxytocin
Outcomes	Caesarean delivery rate (failed induction), duration of labor, maternal and child risks and complications	Bishop score, caesarean delivery rate (failed induction), duration of labor, maternal and child risks and complications	Duration of labor, maternal and child risks and complications	Caesarean delivery rate (failed induction), duration of labor, maternal and child risks and complications
Setting	N/A	Includes any methods used in an outpatient setting	N/A	N/A

Methods

To assess topic nomination 0651, *Induction of Labor,* for priority for a systematic review or other AHRQ EHC report, we used a modified process based on established criteria. Our assessment is hierarchical in nature, with the findings of our assessment determining the need for further evaluation. Details related to our assessment are provided in Appendix A.

1. " Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. " Establish the overall *importance* of a potential topic as representing a health or " healthcare issue in the United States.
3. " Determine the *desirability of new evidence review* by examining whether a new " systematic review or other AHRQ product would be duplicative. "
4. " Assess the *potential impact* a new systematic review or other AHRQ product.
5. " Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. " Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance (see Appendix A).

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews pertaining to the key questions of the nomination. Table 2 includes the citations for the reviews that were determined to address the key questions.

Impact of a New Evidence Review

The impact of a new evidence review was assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether a new review could influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.). See Appendix A.

Feasibility of New Evidence Review

We conducted a literature search in PubMed from August 2010 to August 2016. We reviewed all identified titles and abstracts for inclusion and classified identified studies by study design, to assess the size and scope of a potential evidence review. See Table 2, Feasibility Column, Size/Scope of Review Section for the citations of included studies.

We also searched Clinicaltrials.gov for recently completed or in-process unpublished studies. See Appendix B for the PubMed search strategy and links to the ClinicalTrials.gov search.

Value

We assessed the nomination for value (see Appendix A). We considered whether a partner organization could use the information from the proposed evidence review to facilitate evidence-based change; or the presence of clinical, consumer, or policymaking context that is amenable to evidence-based change.

Compilation of Findings

We constructed a table outlining the selection criteria as they pertain to this nomination (see Appendix A).

Results

Appropriateness and Importance

This is an appropriate and important topic. Induction of labor has merit as a therapeutic option when the benefits of expeditious delivery outweigh the risks of continuing the pregnancy. There are a variety of ways to manage induction of labor and a variety of complications that need to be considered when selecting which methods to use.

Desirability of New Review/Duplication

A new evidence review examining induction of labor would not be duplicative of an existing product. Although we found systematic reviews relevant to all key questions except 1b (methods for inducing labor for women with ruptured membranes) and 3 (fetal surveillance after prostaglandins), there was inconsistency in some of the findings, and there exists no comprehensive review. Our search resulted in 25 completed (14 of which are Cochrane reviews[3-16]) and 3 in-process evidence reviews[17-19] meeting inclusion criteria.

Impact of a New Evidence Review

An AHRQ product on this topic would have moderate impact potential. The standard of care is unclear, and a new review could address knowledge gaps identified in prior systematic reviews. This could influence practice and potentially improve health outcomes, including success of induction of labor.

Feasibility of a New Evidence Review

While published literature is lacking for key questions 1c (methods for inducing labor for women with intrauterine fetal demise in the late second or third trimester), 3 (fetal surveillance after prostaglandins), and 4 (dosage and precautions after oxytocin for induced labor), a new AHRQ evidence review is feasible.

Our search of PubMed resulted in 50 published studies meeting inclusion criteria. We also identified 15 clinical trials relevant to the key questions. We identified 16 studies examining interventions for induction of labor,[20-39] and five examining interventions for induction of labor when there is a ruptured membrane.[40-44] For methods and dosage for administering prostaglandins, we identified six studies.[45-50] 17 studies were identified that examined methods for cervical ripening[37,51-66] Only two studies researching fetal surveillance[67,68] and one study examining oxytocin dosage and precautions[69] were identified in our search.

We identified 15 clinical trials across the key questions. See *Table 2, Feasibility* column for the citations that were determined to address the key questions.

Table 2. Key questions with the identified corresponding evidence reviews and original research

Key Question	Duplication (Completed and In-Process Evidence Reviews)	Feasibility (Published and Ongoing)
KQ 1a: No other co-occurring complicating conditions	Total number of completed or in-progress evidence reviews – 20 • Cochrane – 12[3-14] • Other – 8[70-77]	Published Relevant Studies Identified: 19 • RCT – 16[20-36] • n-RCT – 1[37] • Post Hoc Analysis – 1[38] • Pilot – 1[39] ClinicalTrials.gov Relevant Trials: 2 • Active, not recruiting – 1[78] • Complete – 1[79]
KQ 1b: Ruptured membranes	Total number of completed or in-progress evidence reviews – None identified.	Published Relevant Studies Identified: 5 • RCT – 5[40-44]

Key Question	Duplication (Completed and In-Process Evidence Reviews)	Feasibility (Published and Ongoing)
		ClinicalTrials.gov Relevant Trials: 4 • Recruiting – 3[80-82] • Complete – 1[83]
KQ 1c: Intrauterine fetal demise in the late second or third trimester	Total number of completed or in-progress evidence reviews – 1 • Cochrane – 1[15]	Published Relevant Studies Identified: 0 ClinicalTrials.gov Relevant Trials: 1 • Complete – 1[84]
KQ 2a: Methods and dosage for administering prostaglandins	Total number of completed or in-progress evidence reviews – 22 • Cochrane – 11[3-13] • Other – 8[70-77] • In-Process Other – 3[17-19]	Published Relevant Studies Identified: 6 • RCT – 4[45-48] • Prospective Cohort – 2[49,50] ClinicalTrials.gov Relevant Trials: 2 • Complete – 2[85-87]
KQ 2b: Mechanical or other methods of cervical ripening	Total number of completed or in-progress evidence reviews – 22 • Cochrane – 11[3-13] • Other – 8[70-77] • In-Process Other – 3[17-19]	Published Relevant Studies Identified: 17 • RCT – 14[51-64] • n-RCT – 1[37] • Prospective – 2[65,66] ClinicalTrials.gov Relevant Trials: 4 • Not yet recruiting – 1[88] • Recruiting – 2[89,90] • Complete – 1[87,91]
KQ 3: Fetal surveillance	Total number of completed or in-progress evidence reviews – None identified.	Published Relevant Studies Identified: 2 • Prospective Cohort – 1[67] • Qualitative – 1[68] ClinicalTrials.gov Relevant Trials: None
KQ 4: Oxytocin dosage and precautions	Total number of completed or in-progress evidence reviews – 1 • Cochrane – 1[16]	Published Relevant Studies Identified: 1 • RCT – 1[69] ClinicalTrials.gov Relevant Trials: 1 • Not yet recruiting – 1[92]

Abbreviations: KQ=Key Question; RCT=Randomized Controlled Trial

Value

The potential for value is high, given that ACOG will use a new AHRQ evidence review to inform a clinical practice guideline.

Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
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92. " Zeynep Kamil Maternity and Pediatric Research and Training Hospital. Continuous Versus Intermittent Oxytocin for Induction of Labor: A Randomized Study. *ClinicalTrials.gov.* 2016;NCT02859571.

Appendices

Appendix A: Selection Criteria Summary (

Appendix B: Search Strategy & Results (Feasibility)

Appendix A. Selection Criteria Summary (

Selection Criteria	Supporting Data
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this topic represents a health care drug and intervention available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible. Yes, it is consistent with what is known about the topic.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Yes, this topic represents a significant burden. The CDC states that, "…induction of labor for singleton births reached a high of 23.8% in 2010, then declined in 2011 (23.7%) and 2012 (23.3%)."[1]
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, this topic affects heath care decisions for a large, vulnerable population and there is not a clearly established indication for treatment.
2c. Represents important uncertainty for decision makers	Yes, this topic represents important uncertainty for decision makers.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes, this nomination addresses both the benefits and harms of various interventions of inducing labor.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, this topic represents a common condition, and the increasing medical care costs of its treatments.
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	Although we found systematic reviews relevant to all key questions except 1b (methods for inducing labor for women with ruptured membranes) and 3 (fetal surveillance after prostaglandins), there was inconsistency in some of the findings, and there exists no comprehensive review. Our search resulted in 25 completed (14 of which are Cochrane reviews) and 3 in-process evidence reviews meeting inclusion criteria.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes, the standard of care is unclear, and knowledge gaps may be addressed by a new evidence review.

4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes, there is practice variation.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	While published literature is lacking for key questions 1c (methods for inducing labor for women with intrauterine fetal demise in the late second or third trimester), 3 (fetal surveillance after prostaglandins), and 4 (dosage and precautions after oxytocin for induced labor), a new AHRQ evidence review is feasible. Our search of PubMed resulted in 50 published studies meeting inclusion criteria. We also identified 15 clinical trials relevant to the key questions.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes, this topic exists within a clinical and policy-making context that is amendable to evidence-based change.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Yes ACOG will use the systematic review to inform an clinical practice guideline.

Abbreviations: ACOG= American College of Obstetricians and Gynecologists; AHRQ=Agency for Healthcare Research and Quality; CDC=Centers for Disease Control and Prevention; EHC=Effective Healthcare

Appendix B. Search Strategy & Results (Feasibility)

Source	Evidence
Published primary research studies PubMed/MEDLINE Other applicable databases (e.g., CINAHL, PsycINFO)	**KQ 1a (induction of labor in pregnant women with no co-occurring complications)** • Aalami-Harandi R, Karamali M, Moeini A. Induction of labor with titrated oral misoprostol solution versus oxytocin in term pregnancy: Randomized controlled trial. Rev Bras Ginecol Obstet Feb 2013; 35(2):60-65. • Ajori L, Nazari L, Eliaspour D. Effects of acupuncture for initiation of labor: A double-blind randomized sham-controlled trial. Arch Gynecol Obstet May 2013; 287(5):887-891. • Andersen BB, Knudsen B, Lyndrup J, et al. Acupuncture and/or sweeping of the fetal membranes before induction of labor: A prospective, randomized, controlled trial. J Perinat Med Sep 1 2013; 41(5):555-560. • Carbone JF, Tuuli MG, Fogertey PJ, et al. Combination of foley bulb and vaginal misoprostol compared with vaginal misoprostol alone for cervical ripening and labor induction: A randomized controlled trial. Obstet Gynecol Feb 2013; 121(2 Pt 1):247-252. • Chen W, Zhou Y, Pu X, et al. Evaluation of propess outcomes for cervical ripening and induction of labour in full-term pregnancy. J Obstet Gynaecol Apr 2014; 34(3):255-258. • Edwards RK, Szychowski JM, Berger JL, et al. Foley catheter compared with the controlled-release $ dinoprostone insert: A randomized controlled trial. Obstet Gynecol Jun 2014; 123(6):1280-1287. $ • Jozwiak M, Oude Rengerink K, Ten Eikelder ML, et al. Foley catheter or prostaglandin e2 inserts for induction of labour at term: An open-label randomized controlled trial (probaat-p trial) and systematic review of literature. Eur J Obstet Gynecol Reprod Biol Sep 2013; 170(1):137-145. • Jozwiak M, ten Eikelder M, Oude Rengerink K, et al. Foley catheter versus vaginal misoprostol: Randomized controlled trial (probaat-m study) and systematic review and meta-analysis of literature. Am J Perinatol Feb 2014; 31(2):145-156. • Kehl S, Welzel G, Ehard A, et al. Women's acceptance of a double-balloon device as an additional method for inducing labour. Eur J Obstet Gynecol Reprod Biol May 2013; 168(1):30-35. • Kehl S, Ziegler J, Schleussner E, et al. Sequential use of double-balloon catheter and oral misoprostol versus oral misoprostol alone for induction of labour at term (crbplus trial): A multicentre, open-label randomised controlled trial. BJOG Jan 2015; 122(1):129-136. • Koc O, Duran B, Ozdemirci S, et al. Oxytocin versus sustained-release dinoprostone vaginal pessary for labor induction of unfavorable cervix with bishop score >/= 4 and </= 6: A randomized controlled trial. J Obstet Gynaecol Res Apr 2013; 39(4):790-798. • Lanka S, Surapaneni T, Nirmalan PK. Concurrent use of foley catheter and misoprostol for induction of labor: A randomized clinical trial of efficacy and safety. J Obstet Gynaecol Res Jun 2014; 40(6):1527-1533. • Makarem MH, Zahran KM, Abdellah MS, et al. Early amniotomy after vaginal misoprostol for induction of labor: A randomized clinical trial. Arch Gynecol Obstet Aug 2013; 288(2):261-265. • Neri I, Monari F, Midwife CS, et al. Acupuncture in post-date pregnancy: A pilot study. J Matern Fetal Neonatal Med Jun 2014; 27(9):874-878. • Suffecool K, Rosenn BM, Kam S, et al. Labor induction in nulliparous women with an unfavorable cervix: Double balloon catheter versus dinoprostone. J Perinat Med Mar 2014; 42(2):213-218.

Source	Evidence
	• Teimoori B, Rajabi S, Navvabi-Rigi SD, et al. Evaluation effect of shiatsu technique on labor induction in post-term pregnancy. Glob J Health Sci May 2015; 7(3):177-183. • Ugwu EO, Obi SN, Iferikigwe ES, et al. Membrane stripping to prevent post-term pregnancy in enugu, nigeria: A randomized controlled trial. Arch Gynecol Obstet Jan 2014; 289(1):29-34. **KQ 1b (ruptured membranes)** • Chaudhuri S, Mitra SN, Banerjee PK, et al. Comparison of vaginal misoprostol tablets and prostaglandin e2 gel for the induction of labor in premature rupture of membranes at term: A randomized comparative trial. J Obstet Gynaecol Res Nov 2011; 37(11):1564-1571. • Gungorduk K, Asicioglu O, Besimoglu B, et al. Labor induction in term premature rupture of membranes: Comparison between oxytocin and dinoprostone followed 6 hours later by oxytocin. Am J Obstet Gynecol Jan 2012; 206(1):60 e61-68. • Jha N, Sagili H, Jayalakshmi D, et al. Comparison of efficacy and safety of sublingual misoprostol with intracervical dinoprostone gel for cervical ripening in prelabour rupture of membranes after 34 weeks of gestation. Arch Gynecol Obstet Jan 2015; 291(1):39-44. • Rijal H, Manandhar R, Pradhan N. A randomized study comparing intravaginal prostaglandin (pge2) with oxytocin for induction of labour in premature rupture of membrane at term. Nepal Med Coll J Sep 2012; 14(3):199-203. • van der Ham DP, van der Heyden JL, Opmeer BC, et al. Management of late-preterm premature rupture of membranes: The ppromexil-2 trial. Am J Obstet Gynecol Oct 2012; 207(4):276 e271-210. **KQ 1c (intrauterine fetal demise)** Our search did not yield any studies relevant to this Key Question. **KQ 2 (cervical ripening)** • Abdellah MS, Hussien M, Aboalhassan A. Intravaginal administration of isosorbide mononitrate and misoprostol for cervical ripening and induction of labour: A randomized controlled trial. Arch Gynecol Obstet Jul 2011; 284(1):25-30. • Agarwal K, Batra A, Batra A, et al. Evaluation of isosorbide mononitrate for cervical ripening prior to induction of labor for postdated pregnancy in an outpatient setting. Int J Gynaecol Obstet Sep 2012; 118(3):205-209. • Chen W, Zhou Y, Pu X, et al. Evaluation of propess outcomes for cervical ripening and induction of labour in full-term pregnancy. J Obstet Gynaecol Apr 2014; 34(3):255-258. • Cromi A, Ghezzi F, Agosti M, et al. Is transcervical foley catheter actually slower than prostaglandins in ripening the cervix? A randomized study. Am J Obstet Gynecol Apr 2011; 204(4):338 e331-337. • Cromi A, Ghezzi F, Uccella S, et al. A randomized trial of preinduction cervical ripening: Dinoprostone vaginal insert versus double-balloon catheter. Am J Obstet Gynecol Aug 2012; 207(2):125 e121-127. • Gibson KS, Mercer BM, Louis JM. Inner thigh taping vs traction for cervical ripening with a foley catheter: A randomized controlled trial. Am J Obstet Gynecol Sep 2013; 209(3):272 e271-277.

Source	Evidence
	• Lutgendorf MA, Johnson A, Terpstra ER, et al. Extra-amniotic balloon for preinduction cervical ripening: A randomized comparison of weighted traction versus unweighted. J Matern Fetal Neonatal Med Jun 2012; 25(6):581-586. • Mei-Dan E, Walfisch A, Suarez-Easton S, et al. Comparison of two mechanical devices for cervical ripening: A prospective quasi-randomized trial. J Matern Fetal Neonatal Med Jun 2012; 25(6):723-727. • Mei-Dan E, Walfisch A, Valencia C, et al. Making cervical ripening easi: A prospective controlled comparison of single versus double balloon catheters. J Matern Fetal Neonatal Med Nov 2014; 27(17):1765-1770. • Ten Eikelder ML, Neervoort F, Oude Rengerink K, et al. Induction of labour with a foley catheter or oral misoprostol at term: The probaat-ii study, a multicentre randomised controlled trial. BMC Pregnancy Childbirth 2013; 13:67. • Ugwu EO, Onah HE, Obi SN, et al. Effect of the foley catheter and synchronous low dose misoprostol administration on cervical ripening: A randomised controlled trial. J Obstet Gynaecol Aug 2013; 33(6):572-577. • Vidanagamage RS, Goonewardene IM. The efficacy of two different doses of vaginal isosorbide mononitrate in pre induction cervical ripening: A double blind randomised controlled trial. Ceylon Med J Sep 2011; 56(3):91-100. • Wang W, Zheng J, Fu J, et al. Which is the safer method of labor induction for oligohydramnios women? Transcervical double balloon catheter or dinoprostone vaginal insert. J Matern Fetal Neonatal Med Nov 2014; 27(17):1805-1808. **KQ 2 (outpatient cervical ripening)** • Henry A, Madan A, Reid R, et al. Outpatient foley catheter versus inpatient prostaglandin e2 gel for induction of labour: A randomised trial. BMC Pregnancy Childbirth 2013; 13:25. • Howard K, Gerard K, Adelson P, et al. Women's preferences for inpatient and outpatient priming for labour induction: A discrete choice experiment. BMC Health Serv Res 2014; 14:330. • Schmitz T, Fuchs F, Closset E, et al. Outpatient cervical ripening by nitric oxide donors for prolonged pregnancy: A randomized controlled trial. Obstet Gynecol Dec 2014; 124(6):1089-1097. • Turnbull D, Adelson P, Oster C, et al. Psychosocial outcomes of a randomized controlled trial of outpatient cervical priming for induction of labor. Birth Jun 2013; 40(2):75-80. • Wilkinson C, Bryce R, Adelson P, et al. A randomised controlled trial of outpatient compared with inpatient cervical ripening with prostaglandin e(2) (opra study). BJOG Jan 2015; 122(1):94-104. **KQ 2 (prostaglandins)** • Adeniyi AA, Odukogbe AA, Olayemi A, et al. Randomization of two dosing regimens of vaginal misoprostol for cervical ripening and labor induction in a low resource setting. Niger J Clin Pract May-Jun 2014; 17(3):287-291. • Azubuike IJ, Bassey G, Okpani A. Comparison of 25 and 50 microgram of misoprostol for induction of labour in nulliparous women with postdate pregnancy in port harcourt. Niger J Clin Pract Mar-Apr 2015; 18(2):263-267.

Source	Evidence
	• Ezechukwu PC, Ugwu EO, Obi SN, et al. Oral versus vaginal misoprostol for induction of labor in enugu, nigeria: A randomized controlled trial. Arch Gynecol Obstet Mar 2015; 291(3):537-544. • Rouzi AA, Alsibiani S, Mansouri N, et al. Randomized clinical trial between hourly titrated oral misoprostol and vaginal dinoprostone for induction of labor. Am J Obstet Gynecol Jan 2014; 210(1):56 e51-56. • Sharami SH, Milani F, Faraji R, et al. Comparison of 25 microg sublingual and 50 microg intravaginal misoprostol for cervical ripening and labor: A randomized controlled equivalence trial. Arch Iran Med Oct 2014; 17(10):652-656. **KQ 3 (fetal surveillance after prostaglandins)** • O'Brien E, Rauf Z, Alfirevic Z, et al. Women's experiences of outpatient induction of labour with remote continuous monitoring. Midwifery Apr 2013; 29(4):325-331. • Rauf Z, O'Brien E, Stampalija T, et al. Home labour induction with retrievable prostaglandin pessary and continuous telemetric trans-abdominal fetal ecg monitoring. PLoS One 2011; 6(11):e28129. **KQ4 (oxytocin)** Our search did not yield any studies relevant to this Key Question.
Clinical trials ClinicalTrials.gov http://clinicaltrials.gov/ct2/search	**KQ 1a (induction of labor in pregnant women with no co-occurring complications)** **Completed** • ID: NCT00451308 Title: Induction of labor with a Foley Balloon Catheter: Inflation with 30ml Compared to 60ml Status: Completed, 2009 **Not yet recruiting** • ID: NCT02477085 Title: Methods of Labor Induction and Perinatal Outcomes (MEDIP) Status: Not yet recruiting, last verified, 2015 **KQ 1b (ruptured membranes)** **Completed** • ID: NCT00355303 Title: Comparison of Misoprostol and Prostaglandin E2 (PGE2) Gel for Induction of Labour in Premature Rupture of Membranes at Term Status: Completed, 2013 **Recruiting** • ID: NCT01973036 Title: FOLCROM Trial: Foley Catheter in Rupture of Membranes Status: Recruiting (last verified 2014) • ID: NCT02314728 Title: Cervical Ripening in Premature Rupture of Membranes

Source	Evidence
	Status: Recruiting (last verified 2014) • ID: NCT01916291 Title: Safety and Efficacy of Dinoprostone (Propess) in the Women with Premature Rupture of Membrane and Gestational Age <38 Status: Recruiting (last verified 2013) **<u>KQ 1c (intrauterine fetal demise)</u>** **Completed** • ID: NCT00671060 Title: Misoprostol for Treatment of Fetal Death at 14-28 Weeks of Pregnancy ○ Status: Completed, 2011