**HEALTH EVIDENCE REVIEW COMMISSION (HERC)**

**COVERAGE GUIDANCE: INDUCTION OF LABOR**

**Approved by HERC 8/8/2013; reaffirmed 1/14/2016**

As a part of the coverage guidance monitoring process, the HERC decided on 1/14/2016 (see Appendix D) to reaffirm the existing coverage guidance and reconsider the need to update the topic during the regular two-year review cycle.

## HERC COVERAGE GUIDANCE

Induction of labor is recommended for coverage for the following indications *(strong recommendation)*:

- Gestational age beyond 41 weeks 0 days
- Prelabor rupture of membranes, term
- Fetal demise
- Preeclampsia, term (severe or mild)
- Eclampsia
- Chorioamnionitis

Induction of labor is recommended for coverage for the following indications *(weak recommendation)*:

- Diabetes, pre-existing and gestational
- Placental abruption
- Preeclampsia, preterm (severe or mild)
- Severe preeclampsia, preterm
- Cholestasis of pregnancy
- Preterm, prelabor rupture of membranes;
- Gastroschisis
- Twin gestation
- Maternal medical conditions (e.g., renal disease, chronic pulmonary disease, chronic hypertension, cardiac disease, antiphospholipid syndrome)
- Gestational hypertension
- Fetal compromise (e.g. isoimmunization, oligohydramnios)
- Intrauterine growth restriction/Small for gestational age, term
- Elective purposes, >39 weeks 0 days to <41 weeks 0 days (without a medical or obstetrical indication) with a favorable cervix (for example, with a Bishop score ≥6)

Induction of labor is not recommended for coverage for the following indications *(weak recommendation):*

- Macrosomia (in the absence of maternal diabetes)
- Elective purposes, >39 weeks 0 days to <41 weeks 0 days (without a medical or obstetrical indication) with an unfavorable cervix (for example, a Bishop score <6)
- Intrauterine growth restriction/Small for gestational age, preterm (without other evidence of fetal compromise)

Induction of labor is not recommended for coverage for the following indications *(strong recommendation):*

- Elective purposes <39 weeks (without a medical or obstetrical indication)

Note: Definitions for strength of recommendation are provided in Appendix A GRADE Element Description

## RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

## EVIDENCE SOURCES

American College of Obstetrics and Gynecology (ACOG). (2009). Induction of labor. ACOG Practice Bulletin No. 107, American College of Obstetricians and Gynecologists. *Obstetrics & Gynecology*, *114*, 386-97. Guideline summary available at: http://www.guidelines.gov/content.aspx?id=14884

King, V., Pilliod, R., & Little, A. (2010). *Rapid review: Elective induction of labor*. Portland: Center for Evidence-based Policy. Retrieved February 12, 2013, from http://www.ohsu.edu/xd/research/centers-institutes/evidence-based-policy-center/med/index.cfm

Mozurkewich, E., Chilimigras, J., Koepke, E., Keeton, K., & King, V.J. (2009). Indications for induction of labour: a best-evidence review. *British Journal of Obstetrics and Gynecology, 116*, 626-636.

National Institute for Health and Clinical Excellence (NICE), & National Collaborating Centre for Women's and Children's Health. (2008). Induction of labour. London: RCOG

Press at the Royal College of Obstetricians and Gynaecologists. Retrieved February 12, 2013, from http://guidance.nice.org.uk/CG70/Guidance/pdf/English

The summary of evidence in this document is derived directly from these evidence sources, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

### Clinical Background

The use of induction of labor (IOL) in the U.S. doubled between 1990 and 2006. Rates of labor induction vary substantially from state to state, from a low of 13.2% (California) to a high of 35.2% (Utah). The rate of increase in medically indicated IOL has been slower than the overall increase, suggesting that the increase in elective inductions has been more rapid. The increase in the overall use of induction is likely multifactorial. There appear to have been shifts in the threshold for induction at earlier gestations with both medically indicated and elective IOL. The practices and preferences of individual physicians also have an effect on the use of IOL and the subsequent risk of cesarean delivery. Women's requests may also contribute to increased demand for elective induction of labor (EIOL).

### Evidence Review

*Elective Induction – Maternal Outcomes*
Two systematic reviews of randomized controlled trials found a slight decrease in cesarean delivery with EIOL. A Cochrane review that included three RCTs found that women induced at 37 to 40 (completed) weeks of gestation had a lower risk of cesarean delivery (RR 0.58; 95% CI 0.34-0.99) compared to expectant management. Another systematic review (also including three RCTs, two of which were in the Cochrane review) also reported a decreased risk of cesarean delivery, although it did not reach statistical significance (OR 0.58; 95% CI 0.22-1.50) Similarly, both reviews found an increased risk of operative vaginal delivery, with only one being statistically significant (RR 1.71; 95% CI 1.23-2.39 and OR 1.41; 95% CI 0.83-2.44, respectively). One of these reviews found no difference in perinatal death or stillbirth, while the other did not report this outcome. No other outcomes were reported in these reviews.

Observational studies, on the other hand, using spontaneous labor control groups found an increased risk of cesarean delivery for nulliparous women (six studies) with number needed to harm (NNH) of 4 to 29. However, comparing EIOL to a spontaneous labor control group instead of all women who are not induced but are managed expectantly tends to overestimate the risk of cesarean delivery with EIOL because it does not include those women who develop an indication for IOL, who will have a higher risk of cesarean. Multiparous women may also have an increased risk of cesarean delivery

with a NNH of 62 based on one study, although a second study did not find a significant difference. Two studies, one in multiparas and one in nulliparas, evaluated the influence of Bishop score (a measure of readiness for labor) and the use of preinduction cervical ripening. The Bishop score is calculated as outlined in the table below:

**Bishop Score**

| | Score (points) | | | |
|---|---|---|---|---|
| **Criterion** | **0** | **1** | **2** | **3** |
| Dilation (cm) | 0 | 1-2 | 3-4 | 5-6 |
| Effacement (%) | 0-39 | 40-59 | 60-79 | >80 |
| Fetal Descent | -3 | -2 | -1, 0 | +1, +2 |
| Cervix Consistency | Firm | Medium | Soft | Not applicable |
| Cervix Position | Posterior | Middle | Anterior | Not applicable |

Both studies stated that preinduction cervical ripening was generally used when the Bishop score was less than six. They found conflicting results on the impact of cervical ripening on cesarean section rates, with cervical ripening in multiparous women decreasing risk of cesarean, and in nulliparous women, the use of cervical ripening increased risk of cesarean delivery. Other maternal outcomes reported by these observational studies include the use of epidural anaesthesia, post-partum hemorrhage, maternal fever, perineal tears and a composite measure of postpartum complications. Of these, the only outcomes that found significant differences between the two groups were the use of epidural anaesthesia, which is increased with EIOL, and perineal tears, which are decreased with EIOL. In addition, the one study that reported the composite measure of postpartum complications found that it was increased in patients undergoing EIOL.

*Elective Induction – Neonatal Outcomes*

Other than mortality and stillbirth, neonatal outcomes were only reported in observational studies, which found increased risk of admission to a neonatal intensive care unit (NICU) with EIOL in three of four studies, although only one of these was statistically significant. The fourth study found more admissions to the NICU in the spontaneous labor group, but the difference was not statistically significant. This outcome was only stratified by weeks of gestation in one case series, which found a statistically significantly higher risk when induction occurred at 37 and 38 weeks,

compared to 39 to 41 weeks. Other neonatal outcomes examined included meconium stained amniotic fluid, birth weight, five minute apgar score less than seven, cord blood pH, breastfeeding, use of positive pressure ventilation and neonatal death. Four studies reported on birth weight, and all found small, statistically significant increases in the EIOL group. Three studies found the incidence of meconium stained amniotic fluid to be higher in women undergoing spontaneous labor (two statistically significant), although meconium aspiration syndrome was not reported in any of the studies. Statistically significant differences were not found for any of the other outcomes.

Regarding health service outcomes, five studies reported on the length of labor. Three found a shorter first stage of labor with EIOL, and one found a shorter total length of labor (all statistically significant). The fifth study found that the total time spent on the labor and delivery unit was greater in the EIOL group, although statistical significance was not reported.

*Indications and Contraindications for IOL*

Evidence is sparse for a number of commonly cited indications for IOL. A best evidence review was conducted by Mozurkewich et al in 2009. They found that the only indications for IOL supported by strong evidence of net benefit were gestational age beyond 41 weeks and prelabor rupture of membranes at term.

The only indication for which there was evidence of harm was suspected macrosomia, but there was no evidence of improved fetal outcomes. However, observational studies suggest an increase in the risk of cesarean section.

One additional study was identified in a search of the literature after the date of this best evidence review. An RCT comparing EIOL with expectant management in women with mild preeclampsia or gestational hypertension at term found a lower risk of a composite measure for maternal outcome (mortality, eclampsia, abruption, progression to more severe disease, postpartum hemorrhage) in the EIOL group. There was no significant difference in the risk of cesarean section or admission to the NICU.

There are other indications for IOL that were not addressed in the evidence report, and for which no evidence was found. These include fetal demise, breech presentation and severe preeclampsia at term, as well as a variety of other maternal conditions not specified above.

[Evidence Source]

### Recommendations from Others

The *American College of Obstetrics and Gynecology (ACOG)* identifies specific indications for induction of labor, including but not limited to the conditions listed below:

- Premature rupture of membranes,

- Eclampsia, preeclampsia, gestational hypertension,
- Fetal compromise (severe IUGR, isoimmunization, oligohydramnios),
- Placental abruption,
- Chorioamnionitis,
- Maternal medical conditions (e.g. diabetes, renal disease, chronic pulmonary disease, chronic hypertension, cardiac disease, antiphospholipid syndrome),
- Fetal compromise (e.g., severe fetal growth restriction, isoimmunization, oligohydramnios),
- Post-term pregnancy, and
- Logistical reasons (risk for rapid labor, distance from hospital).

In addition, for patients with gestational diabetes, they state the following:

> No good evidence to support routine delivery before 40 weeks of gestation. There are no data to support a policy of cesarean delivery purely on the basis of GDM. It would appear reasonable to recommend that patients with GDM be counseled regarding possible cesarean delivery without labor when the estimated fetal weight is 4,500 g or greater.

For patients with pregestational diabetes, they state:

> Early delivery may be indicated in some patients with vasculopathy, nephropathy, poor glucose control, or a prior stillbirth. In contrast, patients with well-controlled diabetes may be allowed to progress to their expected date of delivery as long as antenatal testing remains reassuring. Expectant management beyond the estimated due date generally is not recommended. Cesarean delivery may be considered if the estimated fetal weight is greater than 4,500 g in women with diabetes. Induction of labor in pregnancies with a fetus with suspected macrosomia has not been found to reduce birth trauma and may increase the cesarean delivery rate.

For suspected fetal macrosomia, they state:

> Recent large cohort and case–control studies demonstrate the safety of allowing a trial of labor for estimated birth weights of more than 4,000 g. Despite the poor predictive value of an estimated fetal weight beyond 5,000 g and a lack of evidence supporting cesarean delivery at any estimated fetal weight, most, but not all, authors agree that consideration should be given to cesarean delivery in this situation.

For breech presentation, they state:

Mode of delivery should depend on the experience of the healthcare provider. Cesarean will be the preferred mode for most physicians. Planned vaginal delivery may be reasonable. (No comment regarding induction)

[Evidence Source]

The *National Institute for Clinical Excellence (NICE)* has the following recommendations regarding induction of labor:

Induction of labor should be offered in the following circumstances:

- Post-term pregnancy,
- Preterm, prelabor rupture of membranes after 34 weeks,
- Prelabor rupture of membranes at term after 24 hours, and
- Maternal diabetes, any type (after 38 completed weeks gestation).

Induction of labor should not be routinely offered in the following circumstances:

- Maternal request,
- Breech presentation,
- Severe IUGR,
- History of precipitous labor, and
- Suspected macrosomia[1].

Induction of labor may be offered depending on the desires of the patient in the following circumstances:

- Fetal demise.

Indications for which there are contradictory recommendations between ACOG and NICE are the following:

- Severe IUGR,
- History of precipitous labor, and
- Maternal diabetes (after 38 completed weeks gestation).

[Evidence Source]

**Evidence Summary**

[1] Evidence statement to support this recommendation is based on a systematic review of RCTs that found no significant difference between IOL and expectant management on cesarean rates, operative delivery or neonatal outcomes, but non-RCT evidence of increased cesarean section rate, without improvement in neonatal outcomes

Randomized trials suggest that EIOL may decrease the risk of Cesarean section, but increase the risk of operative delivery overall. On the other hand, observational evidence suggests that the risk of cesarean section may be increased with EIOL, particularly in nulliparous women with an unfavorable cervix who undergo EIOL with preinduction cervical ripening, and that it is associated with an increased risk of epidural anaesthesia use and a decreased risk of perineal tearing. Observational evidence also suggests that EIOL may increase the risk of NICU admission for infants, particularly at less than 39 weeks. It also is associated with slightly higher birth weights, and a decreased risk of meconium stained amniotic fluid. EIOL has strong evidence of net benefit for gestational age over 41 weeks and prelabor rupture of membranes, and moderate evidence of net benefit for mild preeclampsia or gestational hypertension at term. Elective IOL for macrosomia is the only indication for which there is evidence of net harm. There are a number of indications for EIOL for which there is insufficient evidence of net benefit or harm. Indications for which there is conflicting recommendations between clinical guidelines include severe IUGR, maternal diabetes and history of precipitous labor.

GRADE FRAMEWORK

The HERC develops recommendations by using the concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE is a transparent and structured process for developing and presenting evidence and for carrying out the steps involved in developing recommendations. There are four elements that determine the strength of a recommendation, as listed in the table below. The HERC reviews the evidence and makes an assessment of each element, which in turn is used to develop the recommendations presented in the coverage guidance box. Balance between desirable and undesirable effects, and quality of evidence, are derived from the evidence presented in this document, while estimated relative costs, values and preferences are assessments of the HERC members.

| Indication | Balance between desirable and undesirable effects | Quality of evidence* | Resource Allocation | Values and preferences | Coverage Recommendation |
|---|---|---|---|---|---|
| Breech | Presumed potential harm exceeds benefit ("considerable risk of maternal and neonatal morbidity" – NICE) | No evidence and unlikely that additional evidence research will be conducted | Less costly than cesarean but risk of major morbidity increasing costs | Limited variability, against IOL | IOL is not recommended for coverage for breech, without other indications for induction<br>*Weak recommendation* |
| Cardiac disease (maternal) | Uncertain tradeoffs (2 case series and 1 poorly done case-control study do not provide sufficient evidence for benefit or harm of IOL) | Very low | Less costly | Moderate variability, would be dependent on the clinical circumstances | IOL is recommended for coverage for women with cardiac disease; there may be clinical circumstances in which benefits outweigh harms that are not captured in the available evidence.<br>*Weak recommendation* |
| Chorioamnionitis | Presumed benefit exceeds harm | No evidence and unlikely that additional evidence research will be conducted | Less costly | Limited variability, most women would choose IOL given risk of severe morbidity | IOL is recommended for coverage<br>*Strong recommendation* |

| Indication | Balance between desirable and undesirable effects | Quality of evidence* | Resource Allocation | Values and preferences | Coverage Recommendation |
|---|---|---|---|---|---|
| Diabetes (gestational and pre-existing) | Uncertain tradeoffs (MED report - 1 RCT found reduced macrosomia at 38 wks (NNT=8), but no difference in patient oriented outcomes (insulin-requiring DM). NICE reports decreased risk of shoulder dystocia (multiple cohort studies), without increased harms (e.g. CS rate); increased risk of stillbirth in pre-existing DM (population inquiry) but unknown if induction decreases stillbirth rate | Moderate | Likely cost neutral, assuming decreased risk of shoulder dystocia | Limited variability, most women would choose IOL given risk of shoulder dystocia and stillbirth. | IOL is recommended for coverage for gestational and pre-existing diabetes *Weak recommendation* |
| Eclampsia (IOL vs. Cesarean) | Uncertain tradeoffs (1 small RCT found reduced maternal length of stay, underpowered, developing country setting) Most of the time C/S will be indicated to expedite delivery, however given the variation in clinical possibilities, IOL may be indicated in limited situations. | Low, and unlikely that additional evidence research will be conducted | Less costly | Limited variabilility, most women would choose immediate delivery using whatever method is most expeditious | IOL is recommended for coverage in eclampsia; delivery is imperative. *Strong recommendation* |
| Elective < 39 weeks | Net harm - increase in NICU admissions based on 3 cohort studies, 1 statistically significant | Low | More costly | Moderate variability, most women would opt against IOL given the increased risk to the fetus, however, many women are interested in early delivery for a variety of reasons | IOL is not recommended for coverage for elective purposes < 39 weeks *Strong recommendation* |

| Indication | Balance between desirable and undesirable effects | Quality of evidence* | Resource Allocation | Values and preferences | Coverage Recommendation |
|---|---|---|---|---|---|
| Elective ≥39 weeks 0 days to 40 weeks 6 days | Unclear; reduced risk of C/S based on RCTs, but observational studies suggest increased risk of C/S, particularly in nulliparous women, and increased risk of NICU admissions | Low | More costly with unfavorable cervix; Less costly with a favorable cervix. | Moderate variability. Some women and clinicians prefer elective deliveries for convenience or maternal intolerance of pregnancy | IOL is recommended for coverage for elective purposes ≥39 weeks 0 days to 40 weeks 6 days in women with a favorable cervix.<br>*Weak recommendation*<br><br>IOL is not recommended for coverage for elective purposes ≥39 weeks 0 days to 40 weeks 6 days in women with an unfavorable cervix.<br>*Weak recommendation* |
| Fetal Demise | Presumed potential benefit (prevents possibility of infection or coagulopathy) | No evidence and unlikely that additional evidence research will be conducted | Less costly due to potential maternal morbidity | No variability. Virtually all women would choose to have IOL. | IOL is recommended for coverage for fetal demise<br>*Strong recommendation* |
| Gastroschisis | Uncertain tradeoffs (1 RCT underpowered to detect most outcomes of interest) | Low | More costly | Moderate variability, would be dependent on the clinical circumstances | IOL is recommended for coverage in gastroschisis; there may be clinical circumstances in which benefits outweigh harms that are not captured in the available evidence.<br>*Weak recommendation* |
| Gestational hypertension | Uncertain | No evidence | More costly | Moderate variability, would be dependent on the clinical circumstances | IOL is recommended for coverage for women with gestational hypertension; there may be clinical circumstances in which benefits outweigh harms.<br>*Weak recommendation* |

| Indication | Balance between desirable and undesirable effects | Quality of evidence* | Resource Allocation | Values and preferences | Coverage Recommendation |
|---|---|---|---|---|---|
| Intrahepatic cholestasis of pregnancy | Uncertain tradeoffs [1 case control study found no diff in outcomes; 1 case series found reduced intrauterine death at 38 wks compared to historical controls (NNT=63)] | Very low and unlikely that additional evidence research will be conducted | More costly | Limited variability. Most women would choose IOL given risk of fetal demise. | IOL is recommended for coverage for intrahepatic cholestasis of pregnancy *Weak recommendation* |
| IUGR/SGA (preterm) | Tradeoffs (1 large RCT found that IOL does not reduce perinatal mortality or longer term disability. Cesarean delivery is reduced with EM) | High | More costly | Moderate variability, would be dependent on the clinical circumstances | IOL is not recommended for coverage for suspected IUGR/SGA in preterm infants without other evidence of fetal compromise *Weak recommendation* |
| IUGR/SGA (term) | Uncertain tradeoffs (1 RCT underpowered found no differences in maternal or fetal outcomes) | Low | More costly | Limited variability most women would choose IOL when clinically indicated | IOL is recommended for coverage as an option for IUGR/SGA at term *Weak recommendation* |
| Macrosomia | Net harm - Does not improve outcomes and may increase Cesarean deliveries | Moderate | Increased costs | Moderate variability, most women would opt against IOL given the increased risk of C/S, however, women are interested in early delivery due to maternal intolerance of pregnancy | IOL is not recommended for coverage for suspected macrosomia *Weak recommendation* |
| Oligohydramnios | Uncertain tradeoffs (small, single RCT found no diff in outcomes between 41 and 42 weeks, but underpowered to detect benefit) | Low | Hospitalization lengthier but compared to increased antenatal monitoring. Likely cost-neutral. | Limited variability, most women would choose IOL if clinically indicated | IOL is recommended for coverage for oligohydramnios *Weak recommendation* |
| Placental Abruption | Uncertain | No evidence | Likely cost neutral or cost saving | Limited variability, most women would choose IOL if clinically indicated | IOL is recommended for coverage for placental abruption *Weak recommendation* |

| Indication | Balance between desirable and undesirable effects | Quality of evidence* | Resource Allocation | Values and preferences | Coverage Recommendation |
|---|---|---|---|---|---|
| Post-term pregnancy (gestational age >41 weeks 0 days) | Net benefit (2 large SRs of 12-16 RCTs found IOL beyond 41 wk 0 days may reduce perinatal mortality and meconium aspiration syndrome. IOL not found to increase cesarean delivery.) | High | Likely cost-saving given benefit/harm ratio | Limited variability, most women would choose IOL given benefits to fetus | IOL is recommended for coverage for post-term pregnancy (gestational age beyond 41 and 0/7 weeks) *Strong recommendation* |
| PPROM (preterm) | Uncertain tradeoffs (single SR with 4 small RCTs found that expedited IOL may reduce chorioamnionitis, but RCTs did not incorporate interventions now considered standard for this condition) | Moderate | IOL would shorten maternal hospitalization but prolong NICU hospitalization, but may prevent significant neonatal complications, likely cost neutral | Moderate variability, would be dependent on the clinical circumstances | IOL is recommended for coverage for PPROM *Weak recommendation* |
| Preeclampsia (mild, term) | Net benefit (1 RCT found lower risk of maternal morbidity) | Moderate | Less costly | Limited variability, most women would choose IOL given maternal benefits | IOL is recommended for coverage for mild preeclampsia at term *Strong recommendation* |
| Preeclampsia (mild, preterm) | Uncertain trade offs | None | Likely cost neutral | Moderate variability, would be dependent on the clinical circumstances | IOL is recommended for coverage for mild preeclampsia (preterm) *Weak recommendation* |
| Preeclampsia (severe, term) | Benefits likely outweigh harms | No evidence | Less costly | Limited variability, most women would choose IOL when clinically indicated | IOL is recommended for coverage for severe preeclampsia in term infants *Strong recommendation* |

| Indication | Balance between desirable and undesirable effects | Quality of evidence* | Resource Allocation | Values and preferences | Coverage Recommendation |
|---|---|---|---|---|---|
| Preeclampsia (severe, <34 weeks, IOL vs. Cesarean) | Uncertain tradeoffs (7 case series found that IOL at 30-34 wks was commonly associated with a cesarean delivery, but that the IOL may help to improve fetal lung maturity compared to cesarean without labor) | Very low | Less costly | Moderate variability, would be dependent on the clinical circumstances | IOL is recommended for coverage above cesarean section for preterm severe preeclampsia, however is not generally recommended above expectant management. *Weak recommendation* |
| Preeclampsia (severe, <34 weeks, IOL vs. EM) | Uncertain tradeoffs (EM for preterm (28-34 wks. in one RCT and 28-32 wks. in the other) severe preeclampsia improves neonatal outcomes, based on 2 small RCTs) | Moderate | More costly | Moderate variability, would be dependent on the clinical circumstances | IOL is recommended for coverage as an option for severe preeclampsia prior to 34 weeks gestation. It appears to be preferable to cesarean section, and there may be clinical circumstances in which benefits of induction outweigh harms that are not captured in the available evidence. *Weak recommendation* |
| Preeclampsia (severe, 34-37 weeks) | Benefits likely outweigh harms | No evidence | Neutral | Limited variability, most women would choose IOL when clinically indicated | IOL is recommended for coverage in severe preeclampsia in preterm infants *Weak recommendation* |
| PROM (term) | Net benefit [3 SRs containing 6-23 RCTs each found expedited IOL (2 to 12 hours after rupture of membranes) reduces maternal infections and neonatal admission to NICU] | High | Likely cost-saving given benefit/harm ratio | Limited variability, most women would choose IOL given risk of infection | IOL is recommended for coverage for PROM at term *Strong recommendation* |

| Indication | Balance between desirable and undesirable effects | Quality of evidence* | Resource Allocation | Values and preferences | Coverage Recommendation |
|---|---|---|---|---|---|
| Twin gestation | Uncertain tradeoffs (1 RCT of IOL at 37 wks for twins underpowered to detect benefit or harm) | Low | Likely less costly on average than elective cesarean, although half would result in CS. | Large variability in preferences. 50% likelihood that second twin will require CS even if first is vaginally delivered. | IOL is recommended for coverage for twin gestation *Weak recommendation* |

* In all cases except for Breech and Fetal Demise, the Quality of Evidence rating was assigned by the primary evidence source, not the Evidence-based Guidelines Subcommittee

Note: GRADE framework elements are described in Appendix A

## POLICY LANDSCAPE

There is a current quality measure developed by the Joint Commission for Accreditation of Hospitals Organization that pertains to elective induction of labor. The measure is titled “Perinatal care: percentage of patients with elective vaginal deliveries or elective cesarean sections at greater than or equal to 37 and less than 39 weeks of gestation completed”. This measure is not currently endorsed by the National Quality Forum. No related measures were found from other entities when searching the National Quality Measures Clearinghouse.

In addition there is a statewide effort to have Oregon hospitals agree to a hard stop on elective induction at 39 and 0 weeks gestation.

## COMMITTEE DELIBERATIONS – EbGS

The Evidence-based Guidelines Subcommittee reviewed the evidence. In the case of induction of labor, the key considerations involved recognizing that all women will have delivery one way or another, that the data on induction only has harm identified for patients electively prior to 39 weeks and in suspected macrosomia. For all other indications there was either evidence of benefit, a suggestion of benefit based on historical case-control or other low quality studies, and considerable patient preference for the opportunity for induction if there would be no increased risk.

Several conditions were moved from weak to strong recommendations (a difference from the algorithm placement) based on committee deliberations. They include: mild and severe preeclampsia at term and eclampsia. These were moved to strong recommendations for coverage based on the fact that there is a considerable risk of major morbidity and delivery is the treatment for these conditions. Breech was left out of the coverage guidance box, because it is not an indication by itself for induction.

There were extensive discussions about elective induction of labor between 39 to 41 weeks. Given that the highest quality evidence reviewed (RCTs) indicated there may be a net benefit of decreased cesarean sections, and the statewide and national efforts focused on the 39 week induction cutoff, the decision was made to make a weak recommendation for coverage for elective inductions with a favorable cervix from 39 to 41 weeks but a weak recommendation against coverage for elective inductions if the cervix was unfavorable (decision supported by RCTs and observational studies which suggested evidence of harm).

## COMMITTEE DELIBERATIONS – VBBS

The VbBS modified the induction of labor guideline for the Prioritized List as follows:

GUIDELINE NOTE 85, INDUCTION OF LABOR

*Line 1*

Induction of labor is covered for:

- Gestational age beyond 41 weeks 0 days
- Prelabor rupture of membranes, term
- Fetal demise
- Preeclampsia, term (severe or mild)
- Eclampsia
- Chorioamnionitis
- Diabetes, pre-existing and gestational
- Placental abruption
- Preeclampsia, preterm (severe or mild)
- Severe preeclampsia, preterm
- Cholestasis of pregnancy
- Preterm, prelabor rupture of membranes;
- Gastroschisis
- Twin gestation
- Maternal medical conditions (e.g., renal disease, chronic pulmonary disease, chronic hypertension, cardiac disease, antiphospholipid syndrome)
- Gestational hypertension
- Fetal compromise (e.g. isoimmunization, oligohydramnios)
- Intrauterine growth restriction/Small for gestational age, term
- Elective purposes, >39 weeks 0 days to <41 weeks 0 days (without a medical or obstetrical indication) with a favorable cervix (for example, with a Bishop score ≥6)

Induction of labor is not covered for the following*:*

- Macrosomia (in the absence of maternal diabetes)
- Elective purposes, >39 weeks 0 days to <41 weeks 0 days (without a medical or obstetrical indication) with an unfavorable cervix (for example, a Bishop score <6)
- Elective purposes <39 weeks (without a medical or obstetrical indication)
- Intrauterine growth restriction/Small for gestational age, preterm (without other evidence of fetal compromise)

## HERC DELIBERATIONS

At its August 8, 2013 meeting, the HERC approved the coverage guidance as referred by EbGS and the revised guideline for the Oregon Health Plan as referred by VbBS.

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

## Appendix A. GRADE Element Descriptions

| Element | Description |
|---|---|
| Balance between desirable and undesirable effects | The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted |
| Quality of evidence | The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted |
| Resource allocation | The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted |
| Values and preferences | The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted |

**Strong recommendation**

***In Favor:*** The subcommittee is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

***Against:*** The subcommittee is confident that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

**Weak recommendation**

***In Favor:*** the subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

***Against:*** the subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

**Quality of evidence across studies for the treatment/outcome**

***High*** = Further research is very unlikely to change our confidence in the estimate of effect.

***Moderate*** = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

***Low*** = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

***Very low*** = Any estimate of effect is very uncertain.

## Appendix B. Applicable Codes

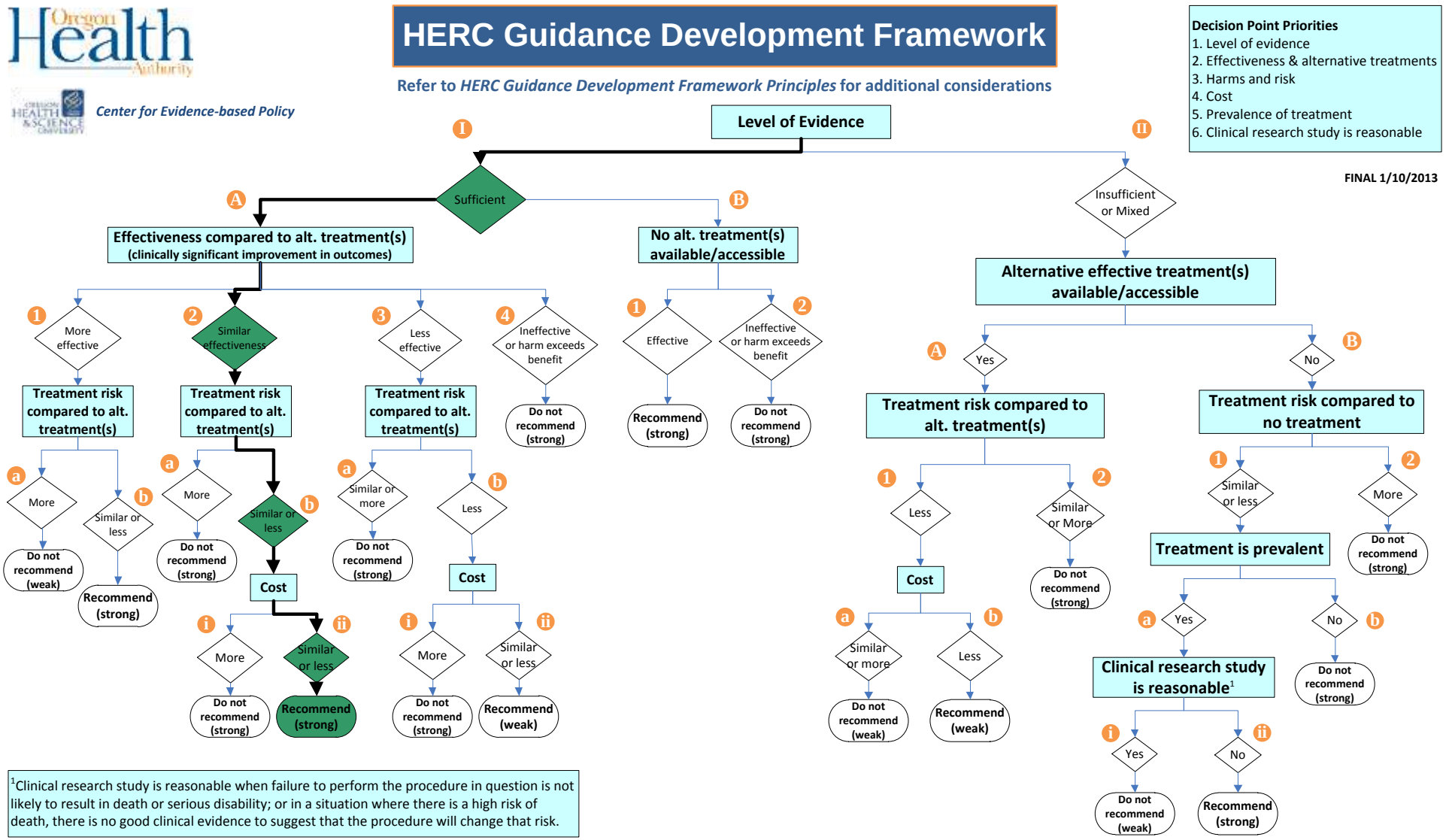
| CODES | DESCRIPTION |
|---|---|
| **ICD-9 Diagnosis Codes** | |
| 650 | Normal delivery |
| 659.0 | Failed mechanical induction |
| 659.1 | Failed medical or unspecified induction |
| V22.0 | Supervision of normal first pregnancy |
| V22.1 | Supervision of other normal pregnancy |
| V22.2 | Pregnant state, incidental |
| V30 | Single liveborn |
| V39 | Liveborn unspecified whether single twin or multiple |
| **ICD-10 Diagnosis Codes** | |
| O80 | Single spontaneous delivery |
| Z34.0 | Supervision of normal first pregnancy |
| Z34.8 | Supervision of other normal pregnancy |
| Z34.9 | Supervision of normal pregnancy, unspecified |
| **ICD-9 Volume 3 (procedure codes)** | |
| **Other procedures inducing or assisting delivery** | |
| 73.0 | Artificial rupture of membranes |
| 73.1 | Other surgical induction of labor: Induction by cervical dilation |
| 73.4 | Medical induction of labor |
| **Forceps, vacuum, and breech delivery** | |
| 72.0 – 72.9 | Forceps, vacuum, and breech delivery |
| **Cesarean section and removal of fetus** | |
| 74.0 – 74.4, 74.9 | Cesarean section and removal of fetus |
| **CPT Codes** | |
| **Dilation** | |
| 57800 | Dilation of cervical canal, instrumental (separate procedure) |
| 59200 | Insertion of cervical dilator (e.g., laminaria, prostaglandin) (separate procedure) |
| **Infusions** | |
| 96365 | Intravenous infusion for therapy, prophylaxis, or diagnosis; initial, up to 1 hour |
| 96366 | Intravenous infusion for therapy, prophylaxis, or diagnosis; each additional hour |
| 96367 | Each additional sequential infusion up to 1 hour |
| 96368 | Concurrent infusion |
| **Care associated with vaginal delivery** | |
| 59400 | Routine obstetric care including antepartum care, vaginal delivery (with or without episiotomy, and/or forceps) and postpartum care |
| 59409 | Vaginal delivery only, with or without postpartum care |
| 59610 | Routine obstetric care including antepartum care, vaginal delivery (with or without episiotomy, and/or forceps) and postpartum care, after previous cesarean delivery |
| 59612, 59614 | Vaginal delivery only, after previous cesarean delivery |
| **Care associated with Cesarean** | |
| 59510 | Routine Obstetric care including antepartum care, Cesarean delivery, and postpartum care |

| | |
|---|---|
| 59514 | Cesarean Delivery only |
| 59515 | Cesarean Delivery only, including postpartum care59618: Routine Obstetric care including antepartum care, Cesarean delivery, and postpartum care, following attempted vaginal delivery after previous cesarean delivery |
| 59620 | Cesarean Delivery only, following attempted vaginal delivery after previous Cesarean delivery. |
| 59622 | Cesarean Delivery only, following attempted vaginal delivery after previous Cesarean delivery. Including postpartum care |
| **HCPCS Level II Codes** | |
| J2590 | Pitocin 10 units. [NOTE: Appears in a listing of "Drugs Administered Other Than Oral Method J0000-J9999."] |
| S0191 | Misoprostol, oral, 200 mcg [NOTE: Appears in a listing of Temporary National Codes (Non-Medicare), S0012-S9999) |

Note: Inclusion on this list does not guarantee coverage

## Appendix C. HERC Guidance Development Framework – IOL Indications

## Post-term Pregnancy (Gestational Age >41 weeks 0 days), PROM (Term) and Maternal Diabetes




[1]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

**PPROM (Preterm), Mild or Severe Preeclampsia, IUGR (term), Gastroschisis, Intrahepatic Cholestasis, Oligohydramnios, Maternal Cardiac Disease, Twins, Placental Abruption, Chorioamnionitis, Gestational Hypertension (Assumes some degree of fetal or maternal compromise), Eclampsia (IOL vs. Cesarean), Elective – Gestational Age 39-41 weeks with favorable cervix**

Oregon Health Authority

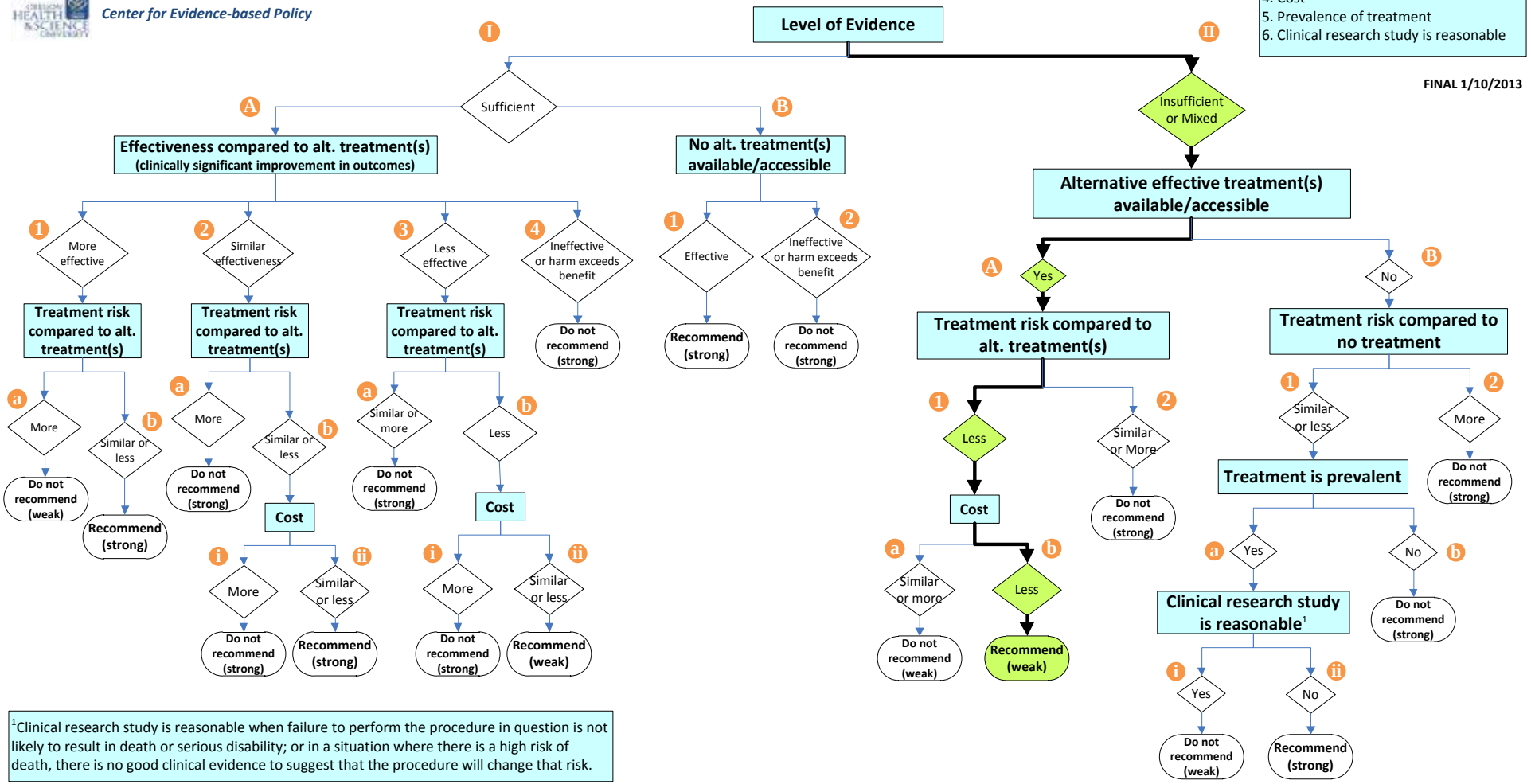
Center for Evidence-based Policy

# HERC Guidance Development Framework

Refer to *HERC Guidance Development Framework Principles* for additional considerations

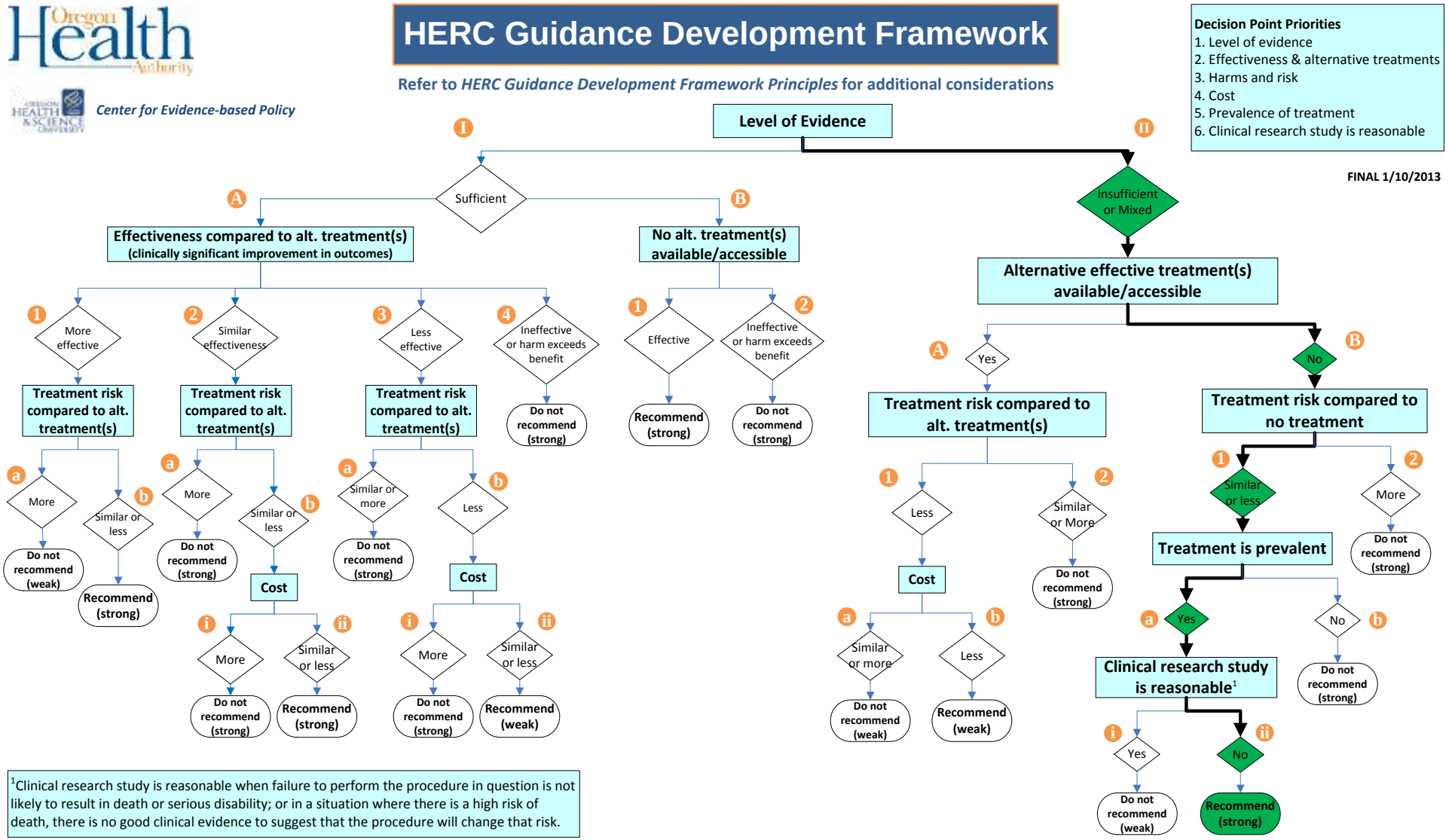
**Decision Point Priorities**
1. Level of evidence
2. Effectiveness & alternative treatments
3. Harms and risk
4. Cost
5. Prevalence of treatment
6. Clinical research study is reasonable

**FINAL 1/10/2013**



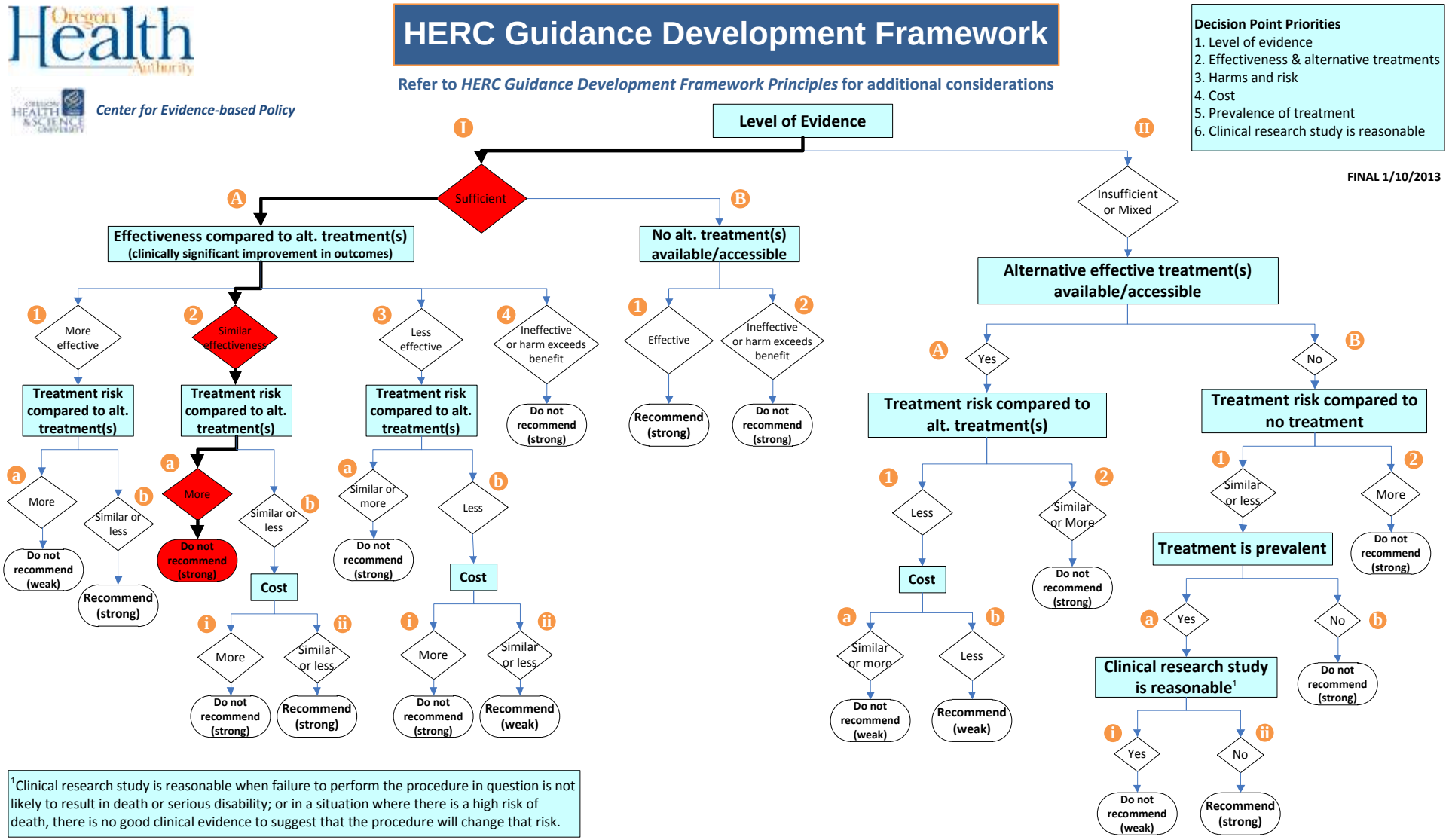

[1]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

## Fetal Demise




[1]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

## Suspected IUGR/SGA (Preterm) and Suspected Macrosomia




[1]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

## Elective – Gestational Age < 39 weeks, Elective – Gestational Age 39-41 weeks with unfavorable cervix

Oregon Health Authority

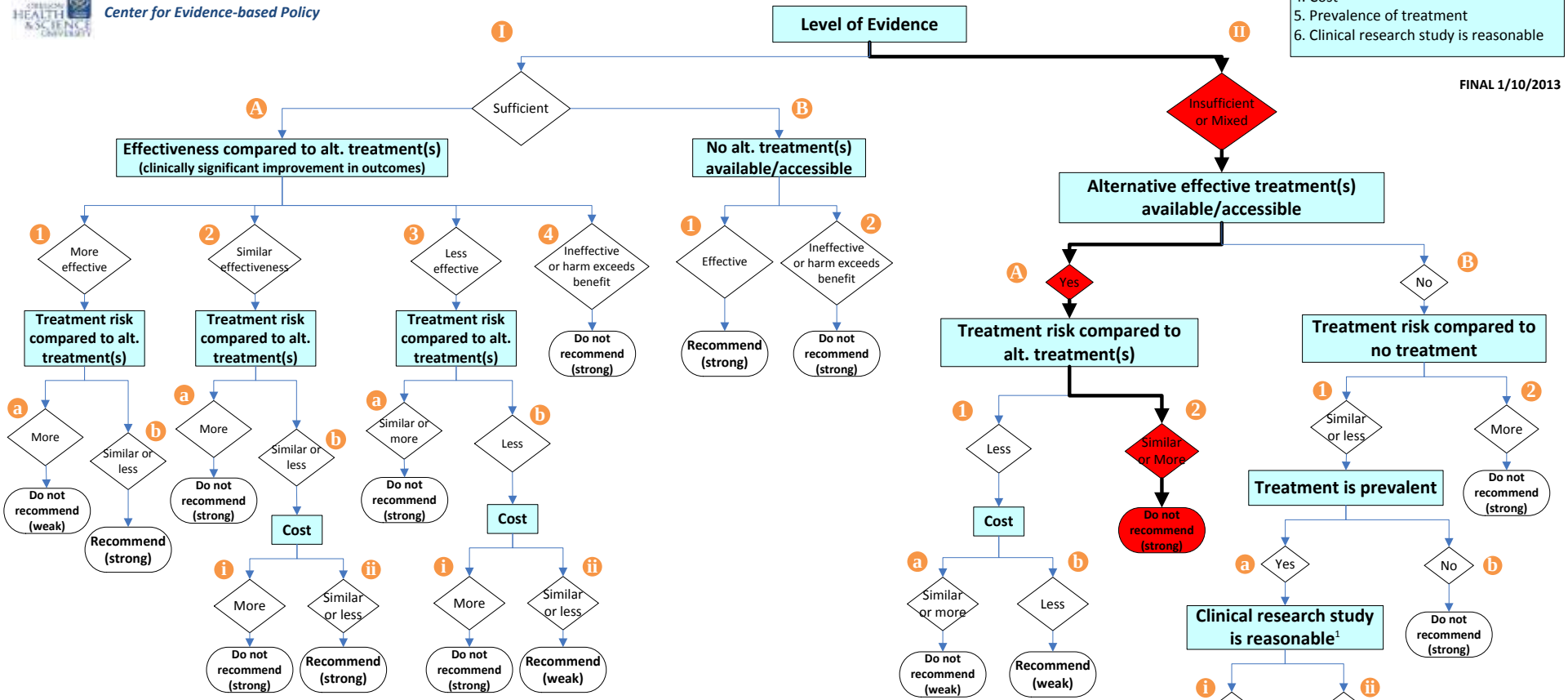
Center for Evidence-based Policy

# HERC Guidance Development Framework

Refer to *HERC Guidance Development Framework Principles* for additional considerations

**Decision Point Priorities**
1. Level of evidence
2. Effectiveness & alternative treatments
3. Harms and risk
4. Cost
5. Prevalence of treatment
6. Clinical research study is reasonable

**FINAL 1/10/2013**




[1]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

## Appendix D: 2015 Rescanning Summary

**HERC Decision (1/14/2016):** Reaffirm the existing coverage guidance and reconsider the need to update the topic during the regular two-year review cycle.

**Bottom Line:** There is little new evidence related to the benefits or harms of induction of labor (IOL). The studies that were identified would not likely result in a change to the HERC coverage guidance issued in 2013.

**Scope Statement**

| | |
|---|---|
| **Population description** | Pregnant adolescents and women<br><br>*Population scoping notes: None* |
| **Intervention(s)** | IOL without medical or obstetrical indications<br><br>*Intervention exclusions: None* |
| **Comparator(s)** | Expectant management |
| **Outcome(s) (up to five)** | **Critical:** Perinatal mortality, maternal mortality, neonatal morbidity<br><br>**Important:** Mode of birth (stratified by indication for operative delivery), maternal length of stay<br><br>*Considered but not selected for GRADE table: Iatrogenic prematurity, hemorrhage, epidural, patient satisfaction, neonatal length of stay* |
| **Key questions** | 1. What are the outcomes of IOL versus expectant management for women without medical or obstetrical indications for induction of labor?<br>2. How do outcomes vary by cervical favorability, gestational age and parity? |
| **Contextual question** | 1. What are the evidence-based medical or obstetrical indications for induction of labor? |

**Scanning Results**

1. Dodd, J. M., Crowther, C. A., Grivell, R. M., & Deussen, A. R. (2014). Elective repeat caesarean section versus induction of labour for women with a previous caesarean birth. *Cochrane Database of Systematic Reviews,* Issue 12. Art. DOI: 10.1002/14651858.CD004906.pub4.

Citation 1 identified no RCTs available to inform management of this population.

2. Dodd, J. M., Deussen, A. R., Grivell, R. M., & Crowther, C. A. (2014). Elective birth at 37 weeks' gestation for women with an uncomplicated twin pregnancy. *Cochrane Database of Systematic Reviews*, Issue 2. Art. DOI: 10.1002/14651858.CD003582.pub2.

Citation 2 identified no new studies since its prior update and had no changes in conclusions. Elective birth at 37 weeks increased the risk of infants being born at less than the third centile of birthweight compared with

expectant management, but there were no other significant differences in maternal or fetal/neonatal outcomes. Current HERC guidance provides a weak recommendation for IOL for twin gestations, but does not specify gestational age restrictions.

3. Gülmezoglu, A. M., Crowther, C. A., Middleton. P/, & Heatley, E. (2012). Induction of labour for improving birth outcomes for women at or beyond term. *Cochrane Database of Systematic Reviews*, Issue 6. Art. DOI: 10.1002/14651858.CD004945.pub3.

The findings of Citation 3 do not change the conclusions of the HERC guidance. Perinatal deaths were lower with IOL at >41 weeks of gestation, but were not significantly different at fewer weeks of gestation. There were fewer cases of meconium aspiration syndrome and macrosomia at 41 and >41 weeks with IOL, but no differences in NICU admission or Apgar score <7 at 5 minutes. Cesarean births were lower with IOL at 41 and >41 weeks, but not significantly different at 37 to 40 weeks of gestation. Operative vaginal births (forceps or vacuum) were more frequent at 37 to 39 weeks with IOL, but not at higher gestational ages. This SR/MA found higher rates of Cesarean birth with “unfavorable” (as defined by study authors, but commonly Bishop Score >6) cervical status, but did not simultaneously control for gestational age or other risk factors.

4. Kaimal, A. J., Little, S. E., Odibo, A. O., Stamilio, D. M., Grobman, W. A., Long, E. F., … Caughey, A. B. (2011). Cost-effectiveness of elective induction of labor at 41 weeks in nulliparous women. *American Journal of Obstetrics and Gynecology, 204*(2), 137.e1-137.e9. DOI: http://dx.doi.org/10.1016/j.ajog.2010.08.012.

Citation 4 is a cost-effectiveness study of eIOL vs. expectant management using a decision-analytic model. Modeling was used rather than a primary economic study done alongside a RCT or other type of study and therefore is subject to the associated usual biases of modeling studies. The analysis found that eIOL at 41 weeks was cost-effective with an incremental cost of $10, 945 per QALY. The authors stated that improved outcomes, including neonatal mortality/morbidity and fewer maternal severe perineal lacerations helped to account for the incremental cost difference.

5. Hussain, A. A., Yakoob, M. Y., Imdad, A., & Bhutta, Z. A. (2011). Elective induction for pregnancies at or beyond 41 weeks of gestation and its impact on stillbirths: a systematic review with meta-analysis. *BMC Public Health, 11*(Supplement 3), S5. DOI: 10.1186/1471-2458-11-S3-S5.

Citation 5 is a SR/MA of eIOL vs. expectant management for pregnancies ≥ 41 weeks of gestation. The SR included 25 studies, of all study designs, and the primary outcome of interest was stillbirth. The authors concluded that eIOL decreases perinatal death overall (RR 0.31, 95% CI 0.11-0.88), but not stillbirth (RR 0.29, 95% CI 0.06-1.38). These findings are in line with evidence considered for the current HERC guidance.

6. Kenny, T. H., Nicodemo, J. M., Fenton, B. W., von Gruenigen, V. E. (2013). Does enhanced "bundling" criteria improve outcomes? A comparative study of elective inductions. *Journal of Reproductive Medicine, 58*(9-10), 402-410. PMID: 24050029.

Citation 6 is a single institution interrupted time series study of an intervention that “bundled” a IHI set of eIOL quality criteria (>=39 weeks, normal fetal status; documentation of all Bishop score components including dilation, effacement, station, cervical position and consistency; and appropriate management of uterine tachysystole during IOL). Adoption of bundling criteria reduced the rate of Cesarean birth (12% vs. 21%), but did not change the rate of NICU admission. However, when the Bishop score was >6 then the rate of Cesarean birth was markedly reduced (4% vs. 19%), as was the rate of NICU admission (1% vs. 10%). The authors concluded that using the IHI eIOL bundle without requiring a specific Bishop score did not achieve

optimal results. The current HERC guidance requires a Bishop score of >=6 for eIOL. This single study does not provide sufficient information to change that cutoff without the addition of other data.

7. Kolkman, D. G., Verhoeven, C. J., Brinkhorst, S. J., van der Post, J. A., Pajkrt, E., Opmeer, B. C., & Mol, B. J. (2013). The Bishop score as a predictor of labor induction success: A systematic review. *American Journal of Perinatology, 30*(8), 625-630. DOI: 10.1055/s-0032-1331024.

Citation 7 looked at the ability of Bishop Scores to predict Cesarean delivery among women undergoing IOL at term. The reported sensitivity/specificity of Bishop Scores of 4, 5 and 6, were 47%-75%, 61%-53%, and 78%-44%, respectively.

8. Mishanina, E., Rogozinska, E., Thatthi, T., Uddin-Khan, R., Khan, K. S., & Meads, C. (2014). Use of labour induction and risk of cesarean delivery: a systematic review and meta-analysis. *CMAJ: Canadian Medical Association Journal, 186*(9), 665-673. DOI: 10.1503/cmaj.130925.

Citation 8 is a SR/MA of RCTs examining the risk of Cesarean birth with IOL. The review found 157 eligible RCTs. The risk of Cesarean birth was overall lower with IOL than expectant management (RR 0.88, 95%CI 0.84-0.93), but the effect was statistically significant for term (37 to <42 weeks) and post-term (>42 weeks) gestations only. Meta-regression demonstrated that initial cervical score, indication for IOL and method of IOL did not change the main result. The risk of fetal death (0.50, 95% CI 0.25-0.99) and admission to a NICU (0.86, 95% CI 0.79-0.94) were lower with IOL, but there was no impact on maternal mortality. This SR/MA included studies using different methods of IOL, with varying indications for IOL, and including women of different term gestational ages, pregnancy risk status, parity and degree of cervical readiness. This SR does not offer new information to the current HERC guidance.

9. NICE. (2014). *Induction of labour. NICE quality standard 60*. London: NICE. Retrieved from http://www.nice.org.uk/guidance/qs60/resources/guidance-induction-of-labour-pdf

Background: NICE. (2014). *Clinical guideline: CG70: Induction of labour. Surveillance report.* London: NICE. Retrieved from http://www.nice.org.uk/guidance/cg70/documents/cg70-induction-of-labour-surveillance-review-decision-may-20142

Background: NICE. (2013). *Induction of labour. Evidence update July 2013. A summary of selected new evidence relevant to NICE clinical guideline 70 'Induction of labor' (2008)*. London: NICE. Retrieved from http://www.nice.org.uk/guidance/cg70/evidence/cg70-induction-of-labour-evidence-update2

The resources listed above in Citation 9 relate to a core source used for the 2013 coverage guidance. NICE conducted surveillance of studies published through December 2013 to determine whether the 2008 IOL guideline should be updated. No new evidence that would impact the guideline was located. The next guideline review is scheduled for 2016.

The second resource represents the quality standards developed by NICE for use in quality of care monitoring and improvement for the NHS. The three quality standards statements relate to: 1) giving personalized information about the benefits and risks of IOL for a woman and her baby when IOL is offered; 2) not conducting outpatient IOL unless safety, support and audit procedures are in place; and 3) providing access to appropriate pain relief for women who are having IOL.

10. Nicholson, J. M., Kellar, L. C., Henning, G. F., Waheed, A., Colon-Gonzalez, M., & Ural, S. (2015). The association between the regular use of preventive labour induction and improved term birth outcomes:

findings of a systematic review and meta-analysis. *BJOG: An International Journal of Obstetrics & Gynaecology, 122*(6), 773-84. DOI: 10.1111/1471-0528.13301.

Citation 10 is a SR/MA re-analysis of four previously published studies of the AMOR-IPAT program of "preventive" IOL at ≥ 38 weeks for women with moderate risk factors such as gestational diabetes, chronic hypertension, etc. These studies were considered in the prior review for the current HERC guidance and this article does not add new information to consideration of guidance update.

11. Rossi, A. C., & Prefumo, F. (2015). Pregnancy outcomes of induced labor in women with previous cesarean section: a systematic review and meta-analysis. *Archives of Gynecology & Obstetrics, 291*(2), 273-80. DOI: 10.1007/s00404-014-3444-9.

Citation 11 is a SR/MA of eight retrospective and one prospective cohort studies of IOL vs. spontaneous labor among women with a history of prior Cesarean birth. This review found that IOL increases the risk of uterine rupture and Cesarean birth, but given the largely retrospective nature of the studies and lack of expectant management control groups this data is of very poor quality and does not add new information to the prior HERC guidance.

12. Teixeira, C., Lunet, N., Rodrigues, T., & Barros, H. (2012). The Bishop Score as a determinant of labour induction success: a systematic review and meta-analysis. *Archives of Gynecology and Obstetrics, 286*(3), 739-753. DOI: 10.1007/s00404-012-2341-3.

Citation 12 was a SR/MA examining the odds of achieving a vaginal birth after IOL. Higher Bishop scores were associated with both vaginal birth and shorter induction to delivery time intervals. For each unit increase in Bishop Score the odds of vaginal birth was increased by 1.33 (95% CI 1.13-1.56), although there was fair heterogeneity among included studies.

13. Vijgen, S. M., Boers, K. E., Opmeer, B. C., Bijlenga, D., Bekedam, D. J., Bloemenkamp, K. W., … Scherjon, S. A. (2013). Economic analysis comparing induction of labour and expectant management for intrauterine growth restriction at term (DIGITAT trial). *European Journal of Obstetrics and Gynecology and Reproductive Biology, 170*(2), 358-363. DOI: 10.1016/j.ejogrb.2013.07.017.

Citation 13 is an alongside economic evaluation conducted with a Dutch RCT of IOL vs. expectant management for suspected IUGR beyond 36 completed weeks of gestation. Both strategies generated comparable costs (7106 euros for IOL vs. 6995 euros for expectant monitoring), although the distribution of antepartum and intrapartum costs differed. Costs were also lower in the expectant management group prior to 38 weeks and in the IOL group after that point. The authors concluded that, given the clinical and economic results of the RCT, that expectant management prior to 38 weeks is a reasonable strategy.

14. Vijgen, S. M., Koopmans, C. M., Opmeer, B. C., Groen, H., Bijlenga, D., Aarnoudse, J. G., … van Pampus, M. G. (2010). An economic analysis of induction of labour and expectant monitoring in women with gestational hypertension or pre-eclampsia at term (HYPITAT trial). *BJOG. An International Journal of Obstetrics and Gynaecology, 117*(13), 1577-1585. DOI: 10.1111/j.1471-0528.2010.02710.x.

Citation 14 is an economic study done in conjunction with a Dutch RCT of IOL vs. expectant management of women with gestational hypertension or pre-eclampsia between 36w + 0d and 41w + 0d of gestation. More costs were generated with expectant monitoring compared to IOL (7908 euros vs 7077 euros). This 11% difference was primarily due to costs originating in the antepartum period. During delivery, more costs were generated by women in the IOL group. There were essentially no differences for costs in the postpartum

period. Given the differences in the systems of care between the Netherlands and the U.S., any direct comparability of costs is not possible.

15. Wood, S., Cooper, S., & Ross, S. (2014). Does induction of labour increase the risk of caesarean section? A systematic review and meta-analysis of trials in women with intact membranes. *BJOG. An International Journal of Obstetrics and Gynaecology, 121*(6), 674-685. DOI: 10.1111/1471-0528.12328.

Citation 15 is a SR/MA of RCTs studying IOL vs. expectant management among women with intact amniotic membranes. Of 37 included studies, 27 included women with uncomplicated pregnancies at 37 to 42 weeks of gestation and the remaining 10 included women with medical and obstetric complications (suspected macrosomia, twins, oligohydramnios, IUGR, hypertension and high risk score for Cesarean birth). The authors concluded that a policy of eIOL reduces the risk of Cesarean birth among women beyond their due dates (OR 0.85, 95% CI 0.76-0.95) and among women with obstetric and medical complications (OR 0.81, 95% CI 0.69-0.95). The odds were similar among both groups when only high quality trials were included, but the CI for the group with complications was no longer statistically significant. The authors noted that only one RCT in the complicated pregnancy group was actually designed to assess the outcome of Cesarean birth and that the effects observed across the included RCTs could, therefore, be due to non-treatment effects and that conclusions based on these data may be premature.

16. World Health Organization (WHO). (2011). *Induction of labour.* Geneva, Switzerland: WHO. Retrieved from http://apps.who.int/iris/bitstream/10665/44531/1/9789241501156_eng.pdf

Citation 16 is largely in alignment with current HERC guidance. The only strong recommendation in the WHO guideline is for IOL among women with prelabor rupture of membrane. There is a weak recommendation for IOL for women at or beyond 41 weeks (41 w. + 0 d.) of gestation. There are weak recommendations against IOL for: 1). women with uncomplicated pregnancy who are less than 41 weeks, 2). including those for whom gestational diabetes is the only abnormality; and 3). women with suspected fetal macrosomia. The WHO panel found insufficient evidence to guide management of women with uncomplicated twin gestation at or near term and so no recommendation was made.

**Summary**

This rescan for the HERC's IOL guidance found evidence that largely comported with and supported existing coverage guidance. Little contradictory or newer evidence was identified that would be likely to change the current coverage recommendations or the strength of those recommendations. The exception is the WHO recommendation against induction without a specific indication for women at fewer than 41 weeks of gestation. The current coverage guidance is silent on the subject of gestational age and IOL for twin pregnancy or pregnancy complicated by gestational hypertension or suspected IUGR. The rescan may have identified studies that could help to identify a target gestational age for expectant monitoring vs. IOL. However, the HERC guidance currently has weak recommendations for these conditions and so largely leaves the decision up to clinical judgment. The rescan identified data confirming that outcomes for eIOL are improved with higher Bishop Score and no need for cervical ripening prior to IOL. The guidance currently recommends a minimum Bishop score of ≥ 6, although some newer evidence indicates that setting a cutoff higher (>6) may improve both maternal and neonatal outcomes. These would not likely be substantial changes to the guidance at present, but the HERC could consider a targeted search relative to each potential indication and modifying factor (such as Bishop Score) at the next rescan. Three economic studies found positive economic results for IOL in the case of gestations over 41 weeks, maternal hypertensive disease and suspected IUGR.

**Methods**

*Search Strategy*
A full search of the core sources was conducted to identify systematic reviews, meta-analyses, technology assessments, and clinical practice guidelines using the terms “induction of labor [or labour],” “elective induction,” and “labor induce.” Searches of core sources were limited to citations published after 2009 (the last search dates of the original evidence sources).

The core sources searched included:

Agency for Healthcare Research and Quality (AHRQ)
Blue Cross/Blue Shield Health Technology Assessment (HTA) program
*BMJ Clinical Evidence*
Canadian Agency for Drugs and Technologies in Health (CADTH)
Cochrane Library (Wiley Interscience)
Hayes, Inc.
Medicaid Evidence-based Decisions Project (MED)
National Institute for Health and Care Excellence (NICE)
Tufts Cost-effectiveness Analysis Registry
Veterans Administration Evidence-based Synthesis Program (ESP)
Washington State Health Technology Assessment Program

A MEDLINE® (Ovid) search was conducted to identify systematic reviews, meta-analyses, and technology assessments published after the search dates of original evidence sources. The search was limited to publications in English published after 2009 (the last search dates of the initial evidence sources).

Searches for clinical practice guidelines were limited to those published since 2010. A search for relevant clinical practice guidelines was also conducted, using the following sources:

Australian Government National Health and Medical Research Council (NHMRC)
Centers for Disease Control and Prevention (CDC) – Community Preventive Services
Institute for Clinical Systems Improvement (ICSI)
National Guidelines Clearinghouse
New Zealand Guidelines Group
NICE
Scottish Intercollegiate Guidelines Network (SIGN)
United States Preventive Services Task Force (USPSTF)
Veterans Administration/Department of Defense (VA/DOD)

*Inclusion/Exclusion Criteria*
Studies were excluded if they were not published in English, did not address the scope statement, or were study designs other than systematic reviews, meta-analyses, technology assessment, or clinical practice guidelines.