

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
 Evaluation of Preterm Labor in Low-risk, Symptomatic Women
 Evidence Summary

Inclusion Criteria:

- Singleton gestation
- 24 weeks, 0 days to 33 weeks 6 days
- No complications that warrant early delivery
- Regular uterine contractions >6 per hour and/or pelvic pressure
- Membranes are intact with no vaginal bleeding
- No evidence of fetal or maternal compromise
- Fetus is alive and viable
- Cervical dilation <3 cm

Exclusion Criteria:

- History of preterm labor or delivery
- Placental abnormalities (abruption and Previa)
- Major fetal anomalies
- Advanced cervical dilation >3 cm
- Uterine malformations
- Cerclage in situ
- Preterm rupture of membranes (PROM)
- Vaginal bleeding/trauma; multi-fetal pregnancy
- Sexual intercourse, a cervical or digital vaginal examination or a transvaginal ultrasound within the last 24 hours

Background

Preterm birth persists as the leading cause of neonatal morbidity and mortality, and the most common reason for antenatal hospitalization. According to the March of Dimes, in 2016 the preterm birth rate for the US was 9.6% and 10.2% for the state of Texas. ⁽¹⁾ According to ACOG, preterm labor is defined as regular contractions of the uterus before 37 weeks of pregnancy and advanced cervical changes. ⁽²⁾ The recognition of women with true symptoms of preterm labor allows for the timely implementation of appropriate interventions to improve neonatal outcomes. On the other hand, accurate triage and evaluation of women who are not in true labor can decrease unnecessary hospitalizations and interventions. The utilization of fetal fibronectin testing allows for the better evaluation of symptomatic women who present with signs and symptoms of labor, and improved targeting of hospital resources. Fetal fibronectin (fFN) is a glycoprotein found in the extracellular matrix of amniotic membranes. ⁽³⁾ It facilitates the attachment of the placenta and amniotic membranes to the uterine decidua. It is normally detectable in cervical secretions from 16 to 20 weeks of gestation. However, the presence of fFN in cervical secretions after 24 weeks of gestation may be indicative of inflammation or the separation of the normal adhesion between the membranes and the uterine decidua. Fetal fibronectin, therefore, plays an important role as an inflammatory marker which often forecasts the onset of preterm labor. The high negative predictive value of the test is well documented in the literature. Additionally, the implementation of fetal fibronectin testing has been shown to be a cost effective method for reducing the number of women being admitted inappropriately for the treatment of preterm labor. Identifying those women at true risk of preterm delivery reduces unnecessary wait times, lab workups, drug infusions, hospital admissions and length of stay.

Critically Analyze the Evidence

The **GRADE criteria** were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence

Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence
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PICO Question 1: In low risk women with sign and symptoms of preterm labor, what is the predictive value of the fetal fibronectin (fFN) test?

Recommendation(s): Strong recommendation with low quality evidence to utilize fetal fibronectin (fFN) test in conjunction with assessment of cervical changes to rule out preterm labor in low risk, symptomatic women. (3-10)

Remarks: The value of fFN testing lies in its negative predictive value. Knowledge of a negative test result, may supplement clinical judgment to predict “false” preterm labor and low risk of imminent preterm birth or preterm delivery in low risk symptomatic women (24 and 34 week, 6 days of gestation, with intact membranes and dilatation <3 cm) within the next 7 to 10 days from testing. Upon digital cervical examination the patient is >3 cm dilated, discard fFN specimen.

In 2008, a Cochrane systematic review analyzed 5 randomized control trials of 474 pregnant women and revealed an association between knowledge of fFN results and a lower incidence of preterm birth before 37 weeks but further research was encouraged. A 2013 systematic review assessed the diagnostic accuracy of the fetal fibronectin test and determined that the test had moderate accuracy for predicting preterm birth but its main potential role is likely to be reducing health care resource usage by identifying women not requiring intervention. Also, evidence from RCTs suggests that fFN does not increase adverse outcomes but may reduce resource use. Honest, et. al. (2002) reviewed 64 observational studies in asymptomatic women and symptomatic women, with a total of 26,876 women. The study revealed that cervicovaginal fetal fibronectin test is most accurate in predicting spontaneous preterm birth within 7-10 days of testing among women with symptoms of threatened preterm. The cervicovaginal fFN assay has limited accuracy in predicting preterm birth within 7 days of sampling in symptomatic pregnant women. Although the test was more sensitive for short-term prediction, its specificity and NPV remains higher than the 80% for the prediction of delivery at <37 weeks’ gestation. 100% of patients with negative result were pregnant at the end of 14 days and 95.5% were still pregnant at the 34 weeks gestation. A negative fFN result is not helpful if cervical dilatation is present, and these patients should be treated as having a high risk of preterm delivery. The use of a fetal fibronectin test was associated with a 90% reduction in maternal transfer and can substantially reduce the costs and inconvenience associated with unnecessary transfer.

Critical Points of Evidence

Evidence Supports

- Utilization of fFN testing to rule out preterm labor in low risk symptomatic women without cervical changes.

Evidence Lacking/Inconclusive

- Any direct effects on cost and resource utilization directly tied to the use of fetal fibronectin testing

Evidence Against

- Utilization of fFN testing alone as a determinant or predictor of preterm labor.

**TCH Evidence Based Outcomes Center
Clinical Algorithm for Evaluation of Preterm Labor in
Low-risk, Singleton, < 3 cm Dilated, Symptomatic Women**

Patient arrival with signs and symptoms of preterm labor
 • Regular uterine contractions (>6 per hr) at EGA 24 weeks 0 days to 33 weeks 6 days
 • Clinical history not suggestive of PROM or placental abruption

Triage Assessment

- History
- Prenatal data
- Assess for signs and symptoms
 - Lower abdominal cramping
 - Pelvic pressure
 - Lower back pain
 - Change in vaginal discharge
 - Painless or painful, but regular uterine activity
- External fetal monitoring
- Psych/social assessment

Physical examination

- Vital signs
- Abdominal examination
- Continuous fetal heart rate and contraction monitoring

Sterile speculum exam

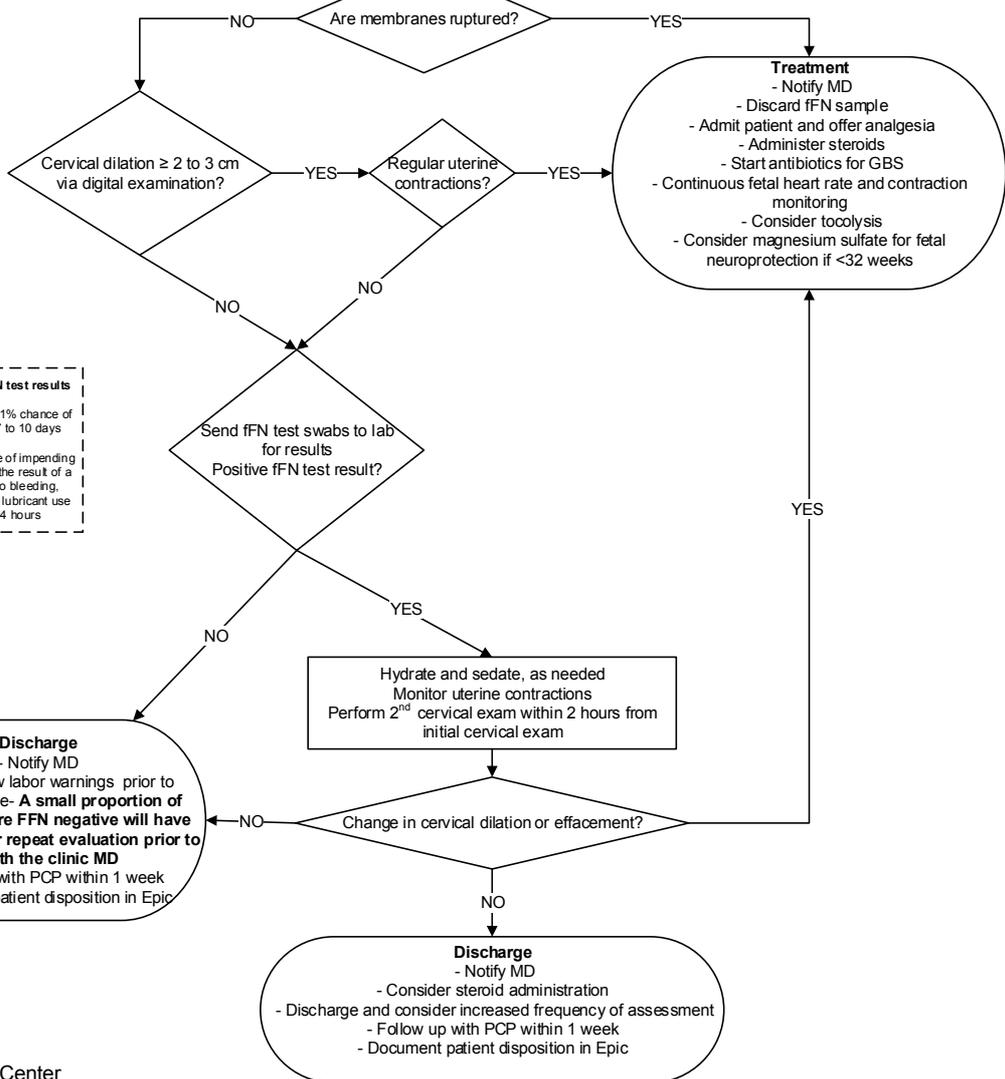
1. Exclude PROM
2. Visualize cervix/membranes
3. Collect fFN swabs prior to pelvic exam
*****Upon visualization if >3 cm dilation and/or bulging membranes noted, do not collect fFN swabs*****
4. Low vaginal/anorectal GBS swab
5. Digital cervical examination

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- No evidence of fetal or maternal compromise
- Fetus is alive and viable
- Cervical dilation < 3cm

Exclusion Criteria:

- Visualization upon speculum exam of >3 cm and/or bulging membranes
- History of preterm labor or delivery
- Placental abnormalities (abruption and Previa)
- Major fetal anomalies
- Advanced cervical dilation >3cm
- Uterine malformations
- Cerclage *in situ*
- Preterm premature rupture of membranes (PPROM)
- Vaginal bleeding/trauma
- Multi-fetal pregnancy
- Sexual intercourse, a cervical or digital vaginal examination or a transvaginal ultrasound within the last 24 hours



Interpretation of fFN test results

Negative= Less than 1% chance of deliver in the next 7 to 10 days

Positive= Inconclusive of impending delivery and may be the result of a false positive due to bleeding, sexual intercourse or lubricant use within the last 24 hours

Discharge

- Notify MD
- RN to review labor warnings prior to discharge home- **A small proportion of patients who are fFN negative will have an indication for repeat evaluation prior to f/u with the clinic MD**
- Follow up with PCP within 1 week
- Document patient disposition in Epic

Discharge

- Notify MD
- Consider steroid administration
- Discharge and consider increased frequency of assessment
- Follow up with PCP within 1 week
- Document patient disposition in Epic

References

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2. ACOG, (2016). Practice Bulletin No. 159 Summary: Management of preterm labor. *Obstetrics & Gynecology*, 127(1), 190-191. doi:10.1097/AOG.0000000000001260.
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11. Sanchez-Ramos, L., Delke, I., Zamora, J. & Kaunitz, A. (2009). Fetal fibronectin as a short-term predictor of preterm birth in symptomatic patients. *American Journal of Obstetrics and Gynecology*, 114(3), 631-640.

Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
 - PICO questions established
 - Evidence search confirmed with content experts
2. Review of Existing Internal and External Guidelines
 - Management of Preterm Labor
 - Preterm Labor Assessment Toolkit
 - Preterm labor and birth
 - Ultrasonographic Cervical Length Assessment in Predicting Preterm Birth in Singleton Pregnancies
3. Literature Review of Relevant Evidence
 - Searched: PubMed and Cochrane
4. Critically Analyze the Evidence
 - 6 meta-analyses, 1 randomized controlled trial, and 10 nonrandomized studies
5. Summarize the Evidence
 - Materials used in the development of the guideline, evidence summary, and order sets are maintained in an evaluation of labor in low-risk, symptomatic women evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of

Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

"Evidence Supports" provides clear evidence that the benefits of the intervention exceed harm.

"Evidence Against" provides clear evidence that the intervention is likely to be ineffective or that it is harmful.

"Evidence Lacking/Inconclusive" indicates there is currently insufficient data or inadequate data to support or refute a specific intervention.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
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Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the evaluation of labor in low-risk, symptomatic women. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care, and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient family, to make the ultimate judgment regarding care.

Version History

Date	Action	Comments
Apr 2017	Originally completed	