The diagnostic accuracy of cervico-vaginal fetal fibronectin in predicting preterm delivery: an overview

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Authors' objectives
To determine the accuracy with which cervico-vaginal foetal fibronectin predicts pre-term delivery.

Searching
MEDLINE was searched from 1966 to April 1996 using the MeSH term 'pregnancy' and the textwords 'fetal' and 'fibronectin'; the search was limited to studies of humans. In addition, the reference lists of all known primary articles and review articles, and recent journal issues were handsearched.

Study selection
Study designs of evaluations included in the review
No inclusion criteria were specified with respect to the study design, and the authors did not describe the design of the included studies.

Specific interventions included in the review
Cervico-vaginal foetal fibronectin before 37 weeks of gestation. For a trial to be included in the meta-analysis, the cut-off point for a positive test result had to be 50 ng.

Reference standard test against which the new test was compared
No inclusion criteria were specified with respect to a reference standard test. Pregnancy outcome (delivery date) serves as the reference standard in all the included primary studies.

Participants included in the review
Pregnant women, symptomatic or asymptomatic for pre-term delivery were included.

Outcomes assessed in the review
Studies reporting pre-term delivery before 37 or 34 weeks of gestation, and delivery within 1 week after testing were eligible for inclusion. Likelihood ratios (LRs) for a positive or negative test were the calculated outcome measures used by the review. The principal analysis was conducted using studies from which 2x2 data of diagnostic test results and pregnancy outcome were obtainable.

How were decisions on the relevance of primary studies made?
Decisions were made independently by two of the authors who were blinded to the study authors, institutional affiliation, language, year of publication and journal. Any disagreements were resolved by consensus or by a third reviewer. The reproducibility of the study selection process was evaluated by calculating the percentage agreement and weighted kappa statistics between the two reviewers.

Assessment of study quality
The internal validity of the studies was evaluated using the following items: recruitment of eligible women; description of diagnostic test (including cut-off level for an abnormal test); blinding of outcome assessment; assessment of gestational age; and completeness of follow-up. Decisions were made independently by two of the authors who were blinded to the study authors, institutional affiliation, language, year of publication and journal. Any disagreements were resolved by consensus or by a third reviewer. The reproducibility of the methodological quality assessment was evaluated by calculating the percentage agreement and weighted kappa statistics between the two reviewers.

Data extraction
The data were abstracted independently by two authors and any disagreements were resolved by conference.

Methods of synthesis
How were the studies combined?
The performance of the test was measured using the LR, i.e. the ratio of the probability of a positive or negative test result in women with pre-term delivery to the probability of the same test result in those without a pre-term delivery, as a summary estimate. A meta-analysis was used to generate pooled LRs by weighting the log LR from each study in inverse proportion to its variance. The pooled LRs were generated for predefined subgroups subjected to the same test using the same cut-off level. The pre-test probabilities (obtained by calculating the overall prevalence of pre-term delivery in the population studied) and LRs were used to calculate post-test probabilities along with 95% confidence intervals (CIs).

How were differences between studies investigated?
The impact of threshold effect was investigated using Spearman's correlation test to evaluate the correlation between true- and false-positive rates. No correlation was identified. Heterogeneity was tested using the Breslow-Day test. The reasons for any differences found were explored further on the basis of variation in methodological quality, using the quality items in a univariate analysis.

Results of the review
A total of 14 trials were included in the meta-analysis: 9 trials of 723 symptomatic women with threatened pre-term labour and 6 trials of 847 asymptomatic women (635 low-risk and 212 high-risk); 1 trial reported both symptomatic and asymptomatic women.

Foetal fibronectin in symptomatic women (threatened pre-term labour). For delivery less than 37 weeks' gestation, the LR was 4.6 (95% CI: 3.5, 6.1) for a positive test and 0.5 (95% CI: 0.4, 0.6) for a negative test. The pre-test probability was 33.7% (95% CI: 30.1, 37.3) given either a positive or negative test result, whereas the post-test probability was 70.2% (95% CI: 63.1, 76.4) for a positive result and 21.0% (95% CI: 17.4, 25.1) for a negative test result. For delivery less than 34 weeks' gestation, the LRs were 2.6 (95% CI: 1.8, 3.7) and 0.2 (95% CI: 0.1, 0.5) for a positive and negative test, respectively. For delivery within 1 week of testing, the LRs were 5.0 (95% CI: 3.8, 6.4) and 0.2 (95% CI: 0.1, 0.4) for a positive and negative test, respectively.

Foetal fibronectin in asymptomatic women at low risk.

For delivery less than 37 weeks' gestation, the LR was 3.2 (95% CI: 2.2, 4.8) for a positive test and 0.8 (95% CI: 0.7, 0.9) for a negative test. The pre-test probability increased from 25.0% (95% CI: 21.7, 28.4) to 52.0% (95% CI: 41.2, 62.6) with a positive test result, but decreased to 22.0% (95% CI: 18.8, 25.5) with a negative result.

Foetal fibronectin in asymptomatic women at high risk.

For delivery less than 37 weeks' gestation, the LR was 2.0 (95% CI: 1.5, 2.6) for a positive test and 0.4 (95% CI: 0.2, 0.8) for a negative test. The pre-test probability increased from 31.5% (95% CI: 23.4, 39.6) to 47.9% (95% CI: 37.0, 59.0) with a positive test result, but decreased to 16.6% (95% CI: 9.4, 27.8) with a negative result. For delivery less than 34 weeks' gestation, the LRs were 2.4 (95% CI: 1.8, 3.2) and 0.6 (95% CI: 0.4, 0.9) for a positive and negative test, respectively.

An exploration of the items of methodological quality as a source of heterogeneity could not provide adequate explanation. Studies with higher methodological quality generally produced more conservative estimates of diagnostic performance. However, the CIs overlapped between subgroups.

Authors' conclusions
The presence of foetal fibronectin in cervico-vaginal mucus has limited accuracy in predicting pre-term delivery, as the LRs for positive and negative results generated only minimal-to-moderate changes in the pre-test probability of pre-term birth. Therefore, decisions regarding the initiation of obstetric interventions for pre-term labour should not be
based solely on the results of this test.

**CRD commentary**

This was a well-structured review with clear inclusion criteria and validity criteria, on which the included studies were judged. The search was relatively limited, even though there were no restrictions on publication language and non-English articles were included, since only MEDLINE was searched. No attempt was made to identify unpublished studies, which raises the possibility of publication bias that may limit the completeness of the review and the reliability of the results. The review methodology was rigorous and well described. The design of the primary studies was not presented clearly in the tables, although elements which relate to the validity of the studies were. No explanation of the risk categories was given, so it is unclear how studies defined which asymptomatic women were at high risk and which were at low risk. The methods used for the data analysis were appropriate, rigorously conducted, and well reported. The authors' conclusions follow from the results presented in the review.

**Implications of the review for practice and research**

**Practice:** The authors state that decisions regarding the initiation of obstetric interventions for pre-term labour should not be based solely on the result of a foetal fibronectin test. They further state that in situations where several diagnostic tests to predict pre-term delivery are available, and where these tests are independent, the LR from the individual tests can be combined by taking their product, and used to produce a combined post-test probability.

**Research:** The authors make no recommendations for further research.

**Bibliographic details**


**PubMedID**

9141580

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Cervix Uteri /chemistry; Female; Fibronectins /analysis; Humans; Mucus /chemistry; Obstetric Labor, Premature /diagnosis; Pregnancy; Sensitivity and Specificity; Vagina /chemistry

**AccessionNumber**

11997000650

**Date bibliographic record published**

30/11/2003

**Date abstract record published**

30/11/2003

**Record Status**

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.