**Authors' objectives**
To assess the cervicovaginal foetal fibronectin test for predicting pre-term delivery.

**Searching**
MEDLINE, Current Contents, and Index Medicus were searched for studies published between 1991 and June 1997. A manual search of the proceedings of perinatal meetings, and of the bibliographies of articles and textbooks was also conducted. Personal communications (presumably with experts in the field) were also undertaken. Studies published in all languages were included.

**Study selection**
Study designs of evaluations included in the review
Prospective cohort studies where the test results were not disclosed to either the women or physicians before delivery, and fewer than 20% of the study participants were excluded from the analysis, were eligible for inclusion.

Specific interventions included in the review
Studies of the cervicovaginal foetal fibronectin test, comprising a kit-based enzyme-linked immunosorbent assay (see Other Publications of Related Interest) and using a cut-off point for a positive result of 50 ng/mL, were eligible for inclusion. Studies using either a single test or multiple tests were included. If multiple tests were performed, women with at least one positive result were considered to have positive test results.

Reference standard test against which the new test was compared
The observed delivery date served as the reference standard for studies included in this review.

Participants included in the review
Studies of pregnant women tested between 20 and 36 weeks' gestation were eligible for inclusion. The included studies were of women at high- and low-risk of pre-term delivery.

Outcomes assessed in the review
No inclusion criteria relating to the outcome measure were specified. Sensitivities, specificities, and positive and negative likelihood ratios (LRs) were the outcome measures used by the review; these were calculated by the authors.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

**Data extraction**
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. Data were extracted on the numbers of participants, proportion delivering pre-term, sampling interval, whether single or multiple tests were used, and the risk status of the study population. The authors assessed the risk status of the population based on its overall pre-term birth rate. The prevalence levels above which the studies were considered as having been conducted in high-risk populations were set before the data were extracted. These were 15, 8 and 5% for delivery before 37, 35 and 34 completed weeks, respectively. The sensitivities, specificities and LRs for positive and negative test results were computed in each study, along with their 95% confidence intervals (CIs).
Methods of synthesis

How were the studies combined?
A random-effects model was used to generate a summary estimate of the LR.

How were differences between studies investigated?
The studies were grouped according to the risk category (high or low) and the number of tests performed (single or multiple). For each stratum, heterogeneity was assessed using the chi-squared test before the summary LR was calculated; a p-value of less than 0.1 was considered statistically significant.

Results of the review

Twenty-nine studies were included: 21 articles and 8 abstracts. Twenty-four of these studies evaluated the foetal fibronectin test to predict pre-term delivery before 37 completed weeks. Four studies involving 3,290 low-risk women evaluated a single-test policy, whilst 5 studies involving 2,752 low-risk women evaluated a multiple-test policy. In high-risk women, there were 12 reports involving 1,591 women who had single tests and 5 studies involving 267 women who had multiple tests. There were 9 studies involving 5,431 women that assessed the prediction of pre-term delivery before 34 or 35 weeks' gestation.

Low-risk populations. Negative LRs were heterogeneous in both single (chi-squared 15.0, p=0.002) and multiple (chi-squared 13.4, p=0.01) test studies. Positive LRs were heterogeneous in studies using multiple tests (chi-squared 8.7, p=0.07). For women who had a single test, the summary positive LR was 7.5 (95% CI: 4.6, 12.3) and the summary negative LR was 0.7 (95% CI: 0.4, 1.0). For women evaluated on a multiple-test policy, the summary positive and negative LRs were 3.0 (95% CI: 2.2, 4.1) and 0.6 (95% CI: 0.4, 0.9), respectively.

High-risk populations.

Positive LRs were heterogeneous for studies using single tests (chi-squared 28.1, p=0.003), while negative LRs were heterogeneous for both single (chi-squared 42.7, p<0.001) and multiple (chi-squared 15.3, p=0.004) test studies. For women who had single tests (risk of pre-term delivery 19.1; 67%) the summary positive and negative LRs were 3.5 (95% CI: 2.6, 4.6) and 0.4 (95% CI 0.3, 0.5), respectively. For women who had multiple tests (risk of pre-term delivery 20.9; 63.8%) the summary positive and negative LRs were 2.7 (95% CI: 2.1, 3.6) and 0.4 (95% CI: 0.2, 0.7), respectively.

Prediction of delivery before 34 or 35 weeks' gestation.

Heterogeneity was present in the positive LRs for low-risk populations, for single tests, and for delivery before 35 weeks (chi-squared 19.6, p<0.001). It was also present in the negative test LRs in high-risk populations, for multiple tests, and for delivery before 34 weeks (chi-squared 5.7, p=0.02). In low-risk single-tested women, the positive and negative LRs were 6.3 (95% CI: 1.9, 20.7) and 0.8 (95% CI: 0.8, 0.9), respectively. In one low-risk multiple test study, the positive LR was 4.5 (95% CI: 3.2, 6.3) and the negative LR was 0.6 (95% CI: 0.5, 0.8). In high-risk single-test populations, the positive and negative LRs were 2.2 (95% CI: 1.6, 3.0) and 0.3 (95% CI: 0.2, 0.6), respectively. In high-risk multiple-test populations, the positive and negative LRs were 2.9 (95% CI: 2.0, 4.2) and 0.3 (95% CI: 0.0, 3.0), respectively.

Authors' conclusions

The presence of foetal fibronectin in cervicovaginal secretions was associated with delivery before 34, 35 or 37 weeks, in both high- and low-risk populations. A negative test result predicted a favourable outcome. These associations were found with both single- and multiple-test strategies. Multiple testing did not improve the overall performance of the test.

CRD commentary

The review addressed a well-defined research question with inclusion criteria that were appropriate and clearly defined.
a priori. A substantial effort was made to search for all the relevant literature, though the search terms used were not reported. The validity of the included studies was not assessed and the review methodology was not described. It is therefore difficult to assess the potential influence of biases, as introduced by deficiencies in the quality of the included studies and in the conduct of the review, on the review's findings. Some limited details of the individual studies were presented. It would, however, have been useful to have included more detail, e.g. participant characteristics.

The authors described the conduct of heterogeneity testing prior to meta-analytic pooling, but the primary studies were combined despite the presence of heterogeneity in some strata. Pooling using a random-effects model does not adequately address the problem of heterogeneity. Further investigation of the sources of heterogeneity would have been desirable.

The authors' conclusions follow from the results, but should be interpreted with caution in view of the limitations described.

Implications of the review for practice and research
Practice: Foetal fibronectin testing may be useful to identify patient subgroups that are suited for evaluation of intervention strategies.

Research: Randomised trials assessing birth testing and intervention programmes must be conducted to determine whether foetal fibronectin screening is beneficial to women and their newborns.

Bibliographic details

PubMedID
9649113

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Cervix Uteri /secretion; Female; Fetus /metabolism; Fibronectins /analysis /metabolism; Humans; Obstetric Labor, Premature /diagnosis /epidemiology; Predictive Value of Tests; Pregnancy; Risk Factors; Vagina /secretion

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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.