How should we test for pre-term labour? An IPD meta-analysis and economic model

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Background

- 60,000 babies are born premature in the UK each year.
- Total cost of this to the public sector is greater than £2.9 billion. The majority of the cost incurred is through hospital stays in the days following birth.
- 80% of women presenting with preterm labour do not give birth within seven days, but nearly all who present with symptoms are admitted.
- Clinical judgement and cervical length using transvaginal ultrasound (TUCL) provide a means of diagnosing woman at risk in UK

“if woman is 30+ weeks pregnant, consider TUCL to determine likelihood of birth within 48 hours
if TUCL is indicated but is not available or not acceptable consider fetal fibronectin testing”.

- Newer, ‘simpler’ testing strategies exist: fetal fibronectin (fFN) tests, quantitative fFN
- Cost-effectiveness of such testing strategies is poorly understood in a UK setting

Aim

Develop a prognostic model including quantitative fetal fibronectin for predicting pre-term labour and assess its cost-effectiveness in UK setting

Methods

IPD meta-analysis

- Explore clinical effectiveness of different prognostic models: clinical judgement, fFN, quantitative fFN, TUCL and other clinical risk factors.
- 5 European studies: Apostel-1, EQUIPP, Eufis, QFCAPS and UCLH. Total 1,783 women with signs of preterm labour.
- Variables included: age, BMI, ethnicity, smoking, nulliparity, multiple pregnancy, gestational age, previous spontaneous preterm delivery <34wks, cervical length and quantitative fFN.
- Multivariable logistic regression modeling used to develop 10 prognostic models.
- Primary outcome was delivery within seven days - clinically important time point.
- Antenatal steroids - which reduce morbidity & mortality in preterm babies - are most effective if delivery occurs within seven days of administration.
- The prognostic models were used to calculate predictive values, from which sensitivity and specificity were calculated.

Economic model

- Based on a UK NHS perspective (cost year 2016) over a 7 day time horizon.

Table 1: Economic model results

<table>
<thead>
<tr>
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<th>Mean Cost (£)</th>
<th>Mean Prob. Correct diagnosis</th>
<th>Mean NMB (£)</th>
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<tr>
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<tr>
<td>Extremely premature model</td>
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<tr>
<td>qfFN</td>
<td>£481 (399,573)</td>
<td>0.889 (0.864,0.911)</td>
<td>£17,301</td>
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<tr>
<td>qfFN + TUCL</td>
<td>£630 (502,790)</td>
<td>0.893 (0.859,0.922)</td>
<td>£17,233</td>
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<tr>
<td>Very premature model</td>
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<tr>
<td>TUCL</td>
<td>£609 (500,743)</td>
<td>0.849 (0.813,0.879)</td>
<td>£16,375</td>
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<tr>
<td>qfFN</td>
<td>£548 (462,650)</td>
<td>0.811 (0.781,0.839)</td>
<td>£15,673</td>
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<tr>
<td>Premature Model</td>
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<tr>
<td>qfFN + TUCL</td>
<td>£609 (439,811)</td>
<td>0.890 (0.843,0.928)</td>
<td>£17,199</td>
</tr>
<tr>
<td>qfFN</td>
<td>£551 (445,675)</td>
<td>0.779 (0.738,0.820)</td>
<td>£15,047</td>
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Methods (continued)

- Predictive value of each diagnostic strategy obtained from the IPD meta-analysis.
- Resource use, unit costs & utilities obtained from published literature.
- Cost per correct diagnosis were calculated as incremental cost-effectiveness ratios (ICERs) & Net Monetary Benefit (NMB).
- Probabilistic analysis based on 1,000 iteration Monte Carlo simulation to address uncertainty in parameter estimates and model outcomes.
- Value of information analysis (VoI) estimated potential value of future research using a time horizon of 10 years, effective population of 2,151,921 women, and the UK threshold of £20,000/QALY.

Results

- qfFN and TUCL (alone or in combination) dominated fFN in all three gestational periods with a lower mean cost per patient and greater probability of correct diagnosis at 7 days.
- The highest NMB varied between qfFN and TUCL (alone or in combination) across all three gestation periods.
- Value of Information analysis showed future research is potentially worthwhile if it costs less than £285 million, £174 million, and £600,000, respectively for to reduce uncertainty in the EP, VP and P model outcomes.

Conclusion

- Our analysis found qfFN to be superior to fFN across all three gestation periods.
- The optimal choice between qfFN and TUCL varies across the three gestation periods.
- NICE recommend TUCL for predicting pre-term labour in women ≥30 weeks pregnant - our findings support this only in Very Premature women.
- TUCL testing requires specialist equipment & clinical expertise so is not routinely available in UK routine practice.
- Our findings suggest that where TUCL is unavailable, qfFN testing should be preferred to fFN as the optimal strategy for predicting pre-term labour.
- Further research is potentially worthwhile to reduce current uncertainty regarding the most cost-effective strategy.

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