Background:
The number of women whose labours are induced is increasing with average rates in England in excess of 20%. A broad range of methods for induction are available, including pharmacological, mechanical and alternative interventions with considerable variation in effectiveness, safety and cost. Of the pharmacological interventions, the most commonly used are prostaglandins. However, even within this class, there is a variety of different prostaglandins, with a variety of modes of administration. The aim of this piece of work is to identify the most cost-effective and safe prostaglandin for cervical ripening and labour induction in the NHS setting.

Methods:
• A network meta-analysis (NMA) of randomised controlled trials (RCTs) was conducted comparing 12 different prostaglandins used for labour induction. Different methods were compared with each other and with no treatment or placebo.
• Data were extracted for five key outcomes in terms of effectiveness and safety: serious neonatal morbidity or perinatal death, serious maternal morbidity or death, uterine hyperstimulation with fetal heart rate changes, failure to achieve vaginal delivery within 24 hours, and caesarean section.
• Relative treatment effects are reported as posterior median odds ratios (OR) and 95% CrI (Credible Intervals). (CI).
• The probability of each treatment being 1st, 2nd, 3rd, etc. most effective was calculated for each outcome.
• All analyses were conducted within a Bayesian framework using OpenBUGS.

Results:
Caesarean section
The complete network of eligible comparisons between treatments for caesarean section is shown in Figure 1. 270 trials were available for inclusion. The nodes represent the number of patients randomized between each pair of treatments and the edges represent the number of studies comparing each pair of treatments.

Figure 1: Network of eligible comparisons for caesarean section

No vaginal delivery within 24 hours
The complete network of eligible comparisons between treatments for no vaginal delivery within 24 hours is shown in Figure 3. 94 trials were available for inclusion.

Figure 3: Network of eligible comparisons for No vaginal delivery within 24 hours

Cost-effectiveness Analysis:
Objective: An economic model is currently being developed with the objective of estimating the cost-effectiveness of the different methods of induction.
Main outcome measure: Cost per Quality Adjusted Life Year (QALY) gained for each method of induction. We will report incremental cost-effectiveness ratios and expected net benefit. The outcomes of the analysis will be plotted on the cost-effectiveness plane and cost-effectiveness acceptability curves will be constructed.
Design: A decision tree analysis incorporating data from the systematic review and NMA, hospital costs, and utilities to quantify health-related quality of life. The expected clinical outcomes and costs in a hypothetical cohort of patients who enter the system of each induction strategy are characterized.

Figure 6: Decision tree representing possible consequences arising from induction of labour

Utility Data
Due to lack of data on maternal and neonatal health outcomes following induction of labour in the literature, we plan to elicit estimates of these from a group of experts using the Visual Analogue Scale. This consists of a continuous scale going from the worst health state imaginable to the best. Respondents are asked to place a mark on the line to indicate how good or bad they perceive each particular health state to be. These estimates will be used in the cost-effectiveness analysis.

Cost Data
The methods of induction compared in this analysis have varying costs. The following are the costs per induction taken from the British National Formulary.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost per Labour Induction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral misoprostol tablet (&lt;50mcg)</td>
<td>£30 (£26.56 – £32)</td>
</tr>
<tr>
<td>Oral misoprostol tablet (≥50mcg)</td>
<td>£26.56 (£20.66 – £32.56)</td>
</tr>
<tr>
<td>Vaginal misoprostol (50mcg or more)</td>
<td>£20.66 (£17.2 – £24.72)</td>
</tr>
<tr>
<td>Intracervical PGE1 gel (200mcg)</td>
<td>£22 (£17.4 – £26.6)</td>
</tr>
<tr>
<td>Intracervical PGE2 pessary (50mcg or more)</td>
<td>£17.4 (£13.5 – £21.3)</td>
</tr>
<tr>
<td>Vaginal misoprostol tablet (50mcg or more)</td>
<td>£17.4 (£13.5 – £21.3)</td>
</tr>
<tr>
<td>Vaginal misoprostol tablet (slow release)</td>
<td>£13.5 (£11.1 – £15.9)</td>
</tr>
<tr>
<td>Vaginal misoprostol tablet (slow release)</td>
<td>£15.9 (£13.5 – £18.3)</td>
</tr>
</tbody>
</table>

However, in order to determine the most cost-effective treatment from the perspective of the NHS and Personal Social Services, the cost of mode of delivery and adverse events must also be taken into account. Data on costs will be taken from NHS reference costs, ensuring that the results are generalisable to other settings. All costs will be expressed in UK pounds sterling.

Conclusion:
• Network meta-analysis provides a unique opportunity to rank the prostaglandin treatments in a coherent, methodologically robust manner, and allows comparisons to be made across outcomes to help guide clinicians and patients to make informed treatment decisions.
• The NMA results show that misoprostol may be the best prostaglandin for labour induction as the titrated dose oral solution appears to be the safest in terms of caesarean section risk, whilst vaginal misoprostol tablets (>50mcg) are the most effective in achieving vaginal delivery within 24 hours of induction. The cost-effectiveness analysis will combine the findings from the NMA with cost and utility data to identify the method of induction that is most cost-effective.
• These findings have important implications for national and international guidelines for induction of labour and future research in this area.