Study of progesterone for the prevention of preterm birth in twins (STOPPIT): findings from a trial-based cost-effectiveness analysis

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study assessed the cost-effectiveness of vaginal progesterone gel for the prevention of spontaneous pre-term birth in twin pregnancies. The authors concluded that progesterone was neither clinically effective nor cost-effective, compared with placebo, in preventing these pre-term births. The methods were satisfactory and the results were comprehensively reported. The authors' conclusions appear to be appropriate for the scope of their analysis.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study assessed the cost-effectiveness of vaginal progesterone gel for the prevention of spontaneous pre-term birth in twin pregnancies. The population was women, with a pregnancy gestation of less than 20 weeks, who were attending specialised antenatal clinics.

Interventions
Progesterone gel (Crinone) was given daily at a dose of 90mg and this was compared with a placebo gel. The gels were administered vaginally at home from 24 weeks gestation.

Location/setting
UK/out-patient and in-patient care.

Methods
Analytical approach:
The evaluation was based on the results from a randomised controlled trial. The authors stated that a health care payer perspective, including only the hospital costs, was used. The time horizon was from randomisation to hospital discharge of both the mother and infant.

Effectiveness data:
The primary clinical outcome was delivery or foetal death before 34 weeks gestation. The efficacy data were from a multicentre randomised, double-blind, placebo-controlled trial entitled the Study of Progesterone for the Prevention of Preterm Birth In Twins (STOPPIT; Norman, et al. 2009, see 'Other Publications of Related Interest' below for bibliographic details). In total, 500 women were enrolled in the study. Three women from each trial arm were lost to follow-up and an intention-to-treat analysis was conducted. The groups were similar in their mean maternal age, mean gestational age at delivery, and number of previous pregnancies.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was pre-term births prevented, which was the reduction in the number of deliveries or foetal deaths before 34 weeks gestation, with the treatment.

Cost data:
The types of resources analysed were the drugs, hospital ward stays (antenatal, labour, and post-natal), neonatal and maternal intensive care admissions, and different modes of delivery (caesarean section, forceps, etc). The hospital costs per episode of care were adjusted for hospital occupancy rates. Data collection forms were used to elicit the resource use from the nine trial hospitals, as well as by face-to-face interviews with clinicians and midwives. The unit costs were from national sources, such as Department of Health Reference Costs, or provided by the trial participating hospitals, while the drug manufacturer (Serono) provided the progesterone costs. The costs of resources were averaged across all trial participants and reported in UK pounds sterling (£). The price year was 2008. Independent sample t-tests were used to assess group differences in resource use and costs, followed by bias-corrected bootstrapping to address skewness.

Analysis of uncertainty:
The overall uncertainty in the costs and effects was tested by creating a sampling distribution, using bootstrap statistics. The results of the bootstrapped analyses were presented in a cost-effectiveness acceptability curve and on the cost-effectiveness plane. One-way sensitivity analyses and a value of information analysis were undertaken and the incremental net benefit was calculated.

Results
The mean hospital costs for the progesterone group, were £28,031.33 (SD 41,599.89) compared with £25,972.07 (SD 38,659.61) for placebo. The mean difference £2,059.25 was not statistically significant (p=0.33); the bootstrap cost difference was £2,334 (95% CI -5,023 to 9,142). The higher costs for the progesterone group were attributed to a greater need for neonatal care and maternal intensive care services.

The percentage of women with pre-term deliveries was 24.7% in the progesterone group versus 19.4% in the placebo group (OR 1.36, 95% CI 0.89 to 2.09).

The base case results did not change when the hospital ward costs were varied and the duration of neonatal hospitalisation in the placebo arm was varied. Bootstrapped analyses of the costs and effects indicated a 20% probability that progesterone was cost-effective at a willingness-to-pay threshold of £30,000 per pre-term birth prevented. At this threshold, there was a net loss to health services of £3,637 (95% CI 3,420 to 3,853). The expected value of perfect information was £1,033,400 based on the number of twin pregnancies per year in England and Wales.

Authors’ conclusions
The authors concluded that progesterone was neither clinically effective nor cost-effective, compared with placebo, for the prevention of pre-term birth in twin pregnancies.

CRD commentary
Interventions:
The vaginal progesterone gel treatment was clearly described, including the dose and administration. This drug might be available in other settings.

Effectiveness/benefits:
The effectiveness data were based on a single prospective randomised controlled trial, at nine centres. The authors provided brief details of the RCT, but some information, such as the method of randomisation, was not reported. A few participants who enrolled in the trial were lost to follow-up and the sample is likely to have been representative of UK women expecting twins. The STOPPIT trial found that progesterone was not effective in reducing the incidence of pre-term delivery. The trial publication should be consulted to assess the validity of these findings (Norman, et al. 2009). The measure of benefit, pre-term births prevented, does not allow comparisons with the benefits of other health care interventions, such as quality-adjusted life-years.

Costs:
The types, quantities, and valuation of the resources were comprehensively reported, with all the data sources and adjustments. The health care resources used by patients outside the hospital before delivery were not included, nor were any long-term costs. This was acknowledged by the authors, but they did not state how this might affect their findings.

Analysis and results:
A net benefit analysis was used to synthesise the incremental costs and incremental effects, for a willingness-to-pay threshold. The results of the joint cost and effect uncertainty analyses were reported in detail, with a graph of the cost and effect pairings on the cost-effectiveness plane. Value of information analysis was used to estimate the value of conducting further research and the findings indicated that the costs of this research would not be justified. The authors provided a discussion of the limitations of their analysis.

Concluding remarks:

The methods were satisfactory and the results were comprehensively reported. The authors’ conclusions appear to be appropriate for the scope of their analysis.

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