Managing perinatal outcomes: the clinical benefit and cost-effectiveness of pharmacologic treatment of recurrent preterm labor

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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.

Health technology
The study compared the use of continuous subcutaneous terbutaline over oral tocolytics following recurrent preterm labour. The average daily terbutaline dose was 3.5 (+/- 1.1) mg for those receiving subcutaneous terbutaline and 234.0 (+/- 9.3) mg for those receiving oral tocolysis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women who had been enrolled by their health care provider in outpatient programmes for a high-risk pregnancy condition. The inclusion criteria were singleton gestation, an initial episode of preterm labour at greater than 20 weeks, and subsequent hospitalisation for recurrent preterm labour at less than 35 weeks. Women who were stabilised and later discharged home following recurrent preterm labour were eligible for the study. The authors excluded those women not prescribed tocolysis and those who experienced medically indicated delivery.

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness and resource use data were collected between April 1995 and January 1999. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness study.

Study sample
It would appear that the sample size was not determined in the planning phase of the study. In addition, no power calculations were performed retrospectively. The study sample was extracted from a large computerised database of clinical data collected from women who had been enrolled in outpatient programmes relating to high-risk pregnancies.
Two treatment groups were then identified from this database, women prescribed oral tocolytics (PO group) and women prescribed subcutaneous terbutaline infusion (SQ group). Each patient in the PO group was matched 1:1 to a patient in the SQ group, so as to control for differences in gestational age at the start of the study period and to provide a better comparison of treatment efficacy. In total, 279 women prescribed oral tocolysis were matched to 279 women prescribed continuous subcutaneous terbutaline following stabilisation of recurrent preterm labour. The mean age of the women was 26.5 (+/- 6.4) years in the PO group and 28.2 (+/- 5.3) years in the SQ group.

Study design
This was a retrospective, 1:1 matched cohort study. The authors did not report the duration of follow-up of the groups. Women with incomplete follow-up were excluded from the analysis.

Analysis of effectiveness
All of the patients included in the study were accounted for in the analysis. The outcomes used were:

- the number of gestational days;
- the proportion of patients achieving at least 37 weeks' gestation;
- the gestational age at delivery;
- the birth weight;
- the proportion of children admitted to a neonatal intensive care unit (NICU; level III);
- the proportion of women having a Caesarean delivery;
- the proportion of children requiring a ventilator; and
- the perinatal and maternal mortality rates.

The two groups were shown to be comparable in terms of age, gravidity, cerclage and gestational age at first preterm labour. However, women in the PO group were significantly more likely to be smokers (9.7% versus 4.3%; p=0.012), and have had a previous preterm delivery (38.0% versus 29.4%; p=0.017) than women in the SQ group. Women in the PO group were also significantly less likely to be married than women in the SQ group (69.2% versus 84.2%; p<0.001).

Effectiveness results
The mean time from recurrent preterm labour to a desired goal of term gestation (37 weeks) was 37.5 (+/- 15.7) days for each group. Women in the SQ group gained an average of 5.5 (95% confidence interval, CI: 2.7 - 8.3) more gestational days than their PO group pair (33.9 +/- 19.0 days versus 28.4 +/- 19.8 days). In the SQ group, 47.3% of women achieved at least 37 weeks' gestation, compared with 38.7% in the PO group, (p=0.045).

Gestational age at delivery was 36.5 (+/- 2.1) weeks in the SQ group and 35.7 (+/- 2.8) weeks in the PO group, (p<0.001). In the SQ group, 2.5% of women had a gestational age of less than 32 weeks, compared with 10.8% in the PO group, (p<0.001).

There were no statistically significant differences in the rates of Caesarean deliveries (15% in the PO group versus 16.5% in the SQ group; p=0.737).

Birth weight was 2,676 (+/- 667) g in the PO group versus 2,943 (+/- 556) g in the SQ group, (p<0.001). In the PO group, 38.0% of children weighed less than 2,500 g, compared with 20.8% of the SQ group, (p<0.001). In the PO group, 6.1% of children weighed less than 1,500 g, compared with 1.4% in the SQ group, (p=0.003).

In the PO group, 26.2% of children had to be admitted to the NICU, compared with 18.6% in the SQ group, (p=0.003).
There were no statistically significant differences in the proportions of children requiring a ventilator (26.3% in the PO group versus 24.2% in the SQ group; p=0.636).

There was one stillborn in the SQ group and no perinatal mortality in the PO group. There were no maternal deaths in either group.

**Clinical conclusions**
The authors concluded that women treated with continuous subcutaneous terbutaline infusion had greater pregnancy prolongation with better neonatal outcomes than women who were treated with oral tocolytics.

**Measure of benefits used in the economic analysis**
The authors did not derive a measure of health benefit. The analysis was therefore categorised as a cost-consequences study.

**Direct costs**
The resource quantities and the costs were reported separately. The direct costs included in the analysis were those of the health service. These costs were for antepartum hospitalisation, outpatient services and nursery days. The estimated cost per day of hospital care combined accommodation and ancillary charges. Physician charges, increased first-year costs and lifetime medical costs were not considered. The estimation of the resource quantities was based on the database used for the effectiveness analysis. The unit costs were derived from hospital charges. It would appear that discounting was, appropriately, not performed. The study reported the average costs. The price year was not reported.

**Statistical analysis of costs**
The costs and resource use quantities were treated stochastically. Data were analysed using Wilcoxon signed rank and McNemar’s tests.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analyses were performed.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The mean antepartum hospitalisation charges were $5,495 (+/- 7,131) in the PO group and $3,986 (+/- 6,895) in the SQ group, (p=0.009).

The mean outpatient service charges were $1,390 (+/- 1,152) in the PO group and $5,520 (+/- 3,292) in the SQ group, (p<0.001).

The mean nursery charges were $15,050 (+/- 32,648) in the PO group and $7,143 (+/- 20,048) in the SQ group.
(p<0.001).

The mean maternal and infant charges were $21,935 (+/- 33,107) in the PO group and $16,649 (+/- 21,707) in the SQ group (difference $5,286; p=0.017).

**Synthesis of costs and benefits**

The costs and benefits were not combined.

**Authors’ conclusions**

In high-risk singleton pregnancies experiencing recurrent preterm labour condition, continuous subcutaneous terbutaline infusion was both a clinically beneficial and cost-effective treatment following recurrent preterm labour.

**CRD COMMENTARY - Selection of comparators**

A justification was given for using oral tocolytics as the comparator. These medications are widely used to treat increased uterine contractions associated with preterm labour, and their use has increased by 50% between 1990 and 1999. You should decide if this is a widely used health intervention in your own setting.

**Validity of estimate of measure of effectiveness**

The analysis was based on a retrospective, 1:1 matched cohort study, which was appropriate for the study question. However, the authors reported that the retrospective design of this analysis, as well as the lack of a placebo control group, limited the generalisability of their study results to other populations. The study sample appears to have been representative of the study population. The patient groups were shown to be comparable in terms of age, gravidity, cerclage and gestational age at first preterm labour. However, women in the PO group were significantly more likely to be smokers and to have had a previous preterm delivery. The authors undertook appropriate statistical tests to determine any significant differences in pregnancy outcomes between the two groups.

**Validity of estimate of measure of benefit**

The authors did not derive a measure of health benefit. The analysis was therefore categorised as a cost-consequences study.

**Validity of estimate of costs**

All the categories of cost relevant to the health service perspective were included in the analysis. The authors reported that physician charges and increased first-year costs were not included in the analysis, neither were charges for hospital observation admissions of less than 24 hours. It is unclear whether these omissions will have affected the authors’ results. The costs and the quantities were reported separately, which will increase the generalisability of the authors’ results. Appropriate statistical analyses of resource use were performed to test for any significant differences between the two groups. The unit costs appear to have been derived from the authors’ settings (i.e. from hospital charges). Appropriate statistical analyses of the costs were again performed to test for significant differences between both groups.

Since the authors did not report the duration of follow-up, it is unclear if discounting was necessary. However, it would appear that the costs were incurred during less than two years. Therefore, if this was the case, discounting was appropriately not performed. Charges were used to proxy prices. Hence, there is the possibility that these charges do not depict the actual costs of both of these interventions. The price year was not reported, which will hamper any possible future inflation exercises.

**Other issues**

The authors made appropriate comparisons of their findings with those from other studies that also found continuous
Subcutaneous terbutaline appeared to be more successful than oral therapy in prolonging gestation. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported that their results were conservative, as they used more conservative estimates for inpatient day care than other estimates reported in the literature. This bias would have favoured the oral tocolytics group since the mean hospital stay was longer than in the subcutaneous group.

**Implications of the study**
From their results and conclusions, the authors appear to recommend the use of subcutaneous terbutaline in the treatment of high-risk singleton pregnancies experiencing recurrent preterm labour.

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None stated.

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

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