17alpha-hydroxyprogesterone caproate for the prevention of preterm delivery: a 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.

Health technology
The study examined the use of 17alpha-hydroxyprogesterone caproate (17HP) for the prevention of preterm delivery (PTD).

Type of intervention
Secondary prevention.

Economic study type
Cost-utility analysis.

Study population
A decision analytic model considered four distinct subgroups of women for use of 17HP:

sub-group 1, prior PTD less than 32 weeks;
sub-group 2, prior PTD 32 - 37 weeks;
sub-group 3, prior term delivery; and
subgroup 4, no prior delivery.

It was assumed that pregnant women with singletons present for prenatal care within the first 16 weeks of gestation.

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

Dates to which data relate
The effectiveness evidence was derived from studies reported between 1975 and 2005. The resource use and cost data were drawn from unpublished data as well as two studies published in 1995 and 2005. The price year was reported to be 2005.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of published studies and estimates of effectiveness based on opinion.

Modelling
The use of a decision tree was not explicitly justified, but it appears to have captured the costs and benefits associated
with treatment appropriately. Data from several sources were combined to evaluate the cost-effectiveness of 17HP.

**Outcomes assessed in the review**
Probability inputs in the model included, for PTD less than 37 weeks and less than 32 weeks:

- the prevention of PTD;
- the probability of PTD;
- the probability of neonatal death (NND); and
- the probability of neonatal morbidity (NNM).

Inputs also included the proportion of primigravid and women with prior term delivery, as well as the proportions with prior PTD of less than 37 weeks and of less than 32 weeks.

**Study designs and other criteria for inclusion in the review**
Not reported. However, only studies reported in the English language were included.

**Sources searched to identify primary studies**
MEDLINE, PubMed and the Cochrane Library were searched. These searches were supplemented by a bibliographic review.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported. However, the level of each study in an evidence hierarchy was reported.

**Number of primary studies included**
The authors reported that 11 primary studies were the sources of the effectiveness evidence.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
No investigation of differences or their potential impact on estimates of effectiveness was reported. The results from the studies appear to have been combined selectively.

**Results of the review**
Probabilities were estimated for each of the outcomes assessed in the review.

The prevention of PTD less than 37 weeks by 17HP was 0.53 (range: 0.37 to 0.65).

The prevention of PTD less than 32 weeks by 17HP was 0.42 (range: 0.09 to 0.63).

The probability of PTD less than 32 weeks was:
0.3 (range: 0.03 to 0.6) in sub-group 1,
0.15 (range: 0.014 to 0.6) in sub-group 2,
0.004 (range: 0.002 to 0.008) in sub-group 3, and
0.008 (range: 0.002 to 0.01) in sub-group 4.
The probability of PTD 32 - 37 weeks was:
0.21 (range: 0.10 to 0.26) in sub-group 1,
0.13 (range: 0.06 to 0.22) in sub-group 2,
0.02 (range: 0.013 to 0.039) in sub-group 3, and
0.054 (range: 0.013 to 0.09) in sub-group 4.
The probability of NND was 0.13 (range: 0.053 to 0.21) given PTD less than 32 weeks, and 0.074 (range: 0.04 to 0.10) given PTD 32 - 27 weeks.
The probability of NNM was 0.55 (range: 0.45 to 0.65) given PTD less than 32 weeks, and 0.25 (range: 0.12 to 0.36) given PTD 32 - 27 weeks.
The model assumed that of the 2 million women who would present per year, 8.7% were multiparous with a prior PTD of less than 37 weeks and 1.3% were multiparous with a prior PTD of less than 32 weeks.

**Measure of benefits used in the economic analysis**
The measures of benefits included the number of PTDs of less than 32 weeks prevented, the number of PTDs of less than 37 weeks prevented, and the quality-adjusted life-years (QALYs). The utility values were derived by applying utility decrements associated with severe, mild or moderate morbidities from a published study (Teng and Wallace 2000, see 'Other Publications of Related Interest' below for bibliographic details) to average US life expectancies. The authors assumed that deliveries at less than 32 weeks were associated with severe morbidities, while those between 32 and 27 weeks were associated with mild to moderate morbidities.

**Direct costs**
Direct medical costs were included and were discounted at a rate of 3% per annum. The costs were derived from a mixture of assumptions, local data and values from the literature. Some quantities were provided, for example, the number of weeks of 17HP per course, depending on the time of previous delivery, and one nurse visit per participant. The costs of hospital admissions secondary to preterm labour were stated to be an average of local setting charge data and values from the literature. These were multiplied by a cost-to-charge ratio to approximate third-party reimbursement. The cost of stay in the neonatal intensive care unit was prorated according to expected duration of admission (not reported). The unit costs were reported. The price year was 2005.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
No indirect costs were included.

**Currency**
Sensitivity analysis
One-way and multi-way sensitivity analyses were performed on the effectiveness, utility and cost estimates. Ranges were stated to be "commensurate with the degree of uncertainty for each point estimate". It was unclear whether they were derived from the same sources as the point estimates or if they represented author assumptions.

Estimated benefits used in the economic analysis
Estimated QALYs gained were:

- 68.7 with 17HP and 63.2 without in sub-group 1 (difference 5.5);
- 70.6 with 17HP and 67.9 without in sub-group 2 (difference 2.7);
- 72.6 with 17HP and 72.5 without in sub-group 3 (difference 0.1); and
- 72.5 with 17HP and 72.2 without in sub-group 4 (difference 0.3).

In the cohort of 2 million women, the numbers of NND averted using 17HP were:

- 108 less than 32 weeks and 161 less than 37 weeks in sub-group 1;
- 182 less than 32 weeks and 566 less than 37 weeks in sub-group 2;
- 397 less than 32 weeks and 1,853 less than 37 weeks in sub-group 3; and
- 12 less than 32 weeks and 54 less than 37 weeks in sub-group 4.

The numbers of NNM averted using 17HP were:

- 450 less than 32 weeks and 536 less than 37 weeks in sub-group 1;
- 769 less than 32 weeks and 1,889 less than 37 weeks in sub-group 2;
- 1,679 less than 32 weeks and 6,183 less than 37 weeks in sub-group 3; and
- 49 less than 32 weeks and 181 less than 37 weeks in sub-group 4.

Cost results
The total costs were:

- $13,000 with 17HP and $30,000 without in sub-group 1 (difference $17,000);
- $7,000 with 17HP and $15,000 without in sub-group 2 (difference $8,000);
- $755 with 17HP and $582 without in sub-group 3 (difference $173); and
- $1,810 with 17HP and $1,104 without in sub-group 4 (difference $706).

The total cost results for each strategy within sub-groups 3 and 4 appear to have been reversed when entered into the table of results; what appear to be the "correct" results are reported here.

The total costs for 2 million women were calculated to be $107.9 million in sub-group 1, $331.9 million in sub-group 2, $3,433 million in sub-group 3 and $100.6 million in sub-group 4.
Synthesis of costs and benefits
The estimated benefits and costs were combined in average and incremental cost-effectiveness ratios.

In the cost-utility analysis, 17HP was shown to dominate in sub-groups 1 and 2 (i.e. the strategy was associated with lower costs and better QALY outcomes). The incremental cost-effectiveness ratios for the other two sub-groups were $1,730 per QALY gained (sub-group 3) and $2,353 per QALY gained (sub-group 4).

The costs per additional PTD less than 37 weeks averted using 17HP were $35,319 in sub-group 1, $36,093 in sub-group 2, $129,991 in sub-group 3 and $130,649 in sub-group 4. It was stated that the costs per additional PTD less than 32 weeks averted using 17HP was most favourable, at $95,402 in sub-group 1.

The average cost per NND averted was lowest in sub-group 1, while the average cost per NNM averted was lowest in sub-group 2.

The model was robust to almost all parameters evaluated in the sensitivity analysis, but universally sensitive to the efficacy of 17HP in preventing PTD less than 32 weeks. When this probability was greater than 31.5% in women using 17HP, the "no 17HP" strategy became more cost-effective.

Authors' conclusions
The use of 17alpha-hydroxyprogesterone caproate (17HP) was found to be cost-effective, and even cost-saving, in terms of quality-adjusted life-year (QALY) gains for women with prior preterm births. It may also be cost-effective in patient groups without a history of preterm delivery (PTD). Cost-effectiveness with respect to other outcomes, such as preterm births avoided, would depend on society's willingness-to-pay for these outcomes. However, the authors would expect this to be high given the significant contribution of preterm birth to neonatal mortality and morbidity.

CRD COMMENTARY - Selection of comparators
The choice of the comparator (do nothing) was implicitly justified as representing current practice in the authors' setting. You should decide whether this is a relevant comparator in your own setting.

Validity of estimate of measure of effectiveness
The authors stated that a systematic review of the literature had been undertaken, but it was unclear whether the review was conducted in a systematic way to identify relevant research and minimise biases. It was also unclear how the estimates of effectiveness from different studies were combined. The authors did not consider the impact of differences among the primary studies when estimating effectiveness.

Validity of estimate of measure of benefit
The estimation of benefits (QALYs, preterm births averted etc.) was modelled. The decision analytic model used was appropriate for the study question.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted appear to have been included, although it was unclear whether all the relevant costs were included because some costs and quantities, particularly for hospital admissions, were insufficiently separated and reported. However, the additional costs of 17HP appear to have been included appropriately. If differences in hospital admission costs were not adequately captured, there might have been some impact on the results, although the conclusions may or may not have been affected. Resource use and prices were averaged from published studies and local data. A sensitivity analysis of the quantities was not conducted and this may limit the interpretation of the findings. A sensitivity analysis around the prices was conducted. The authors did not clearly explain why they applied a cost-to-charge ratio to hospital charges in relation to the study perceptive.
Other issues
The authors made appropriate comparisons of their findings with those from other studies, noting that this was the first study to consider costs and quality of life associated with preterm birth over a lifetime horizon. The issue of generalisability to other settings was not addressed. The authors appear to have presented their results selectively. For example, it was unclear why an average and not incremental cost-effectiveness analysis was reported for the NND and NNM outcomes, while incremental cost-effectiveness ratios for the outcomes of preterm deliveries avoided were not reported fully within the text and were not tabulated. The authors’ conclusions reflected the scope of the analysis and were sufficiently cautious with respect to the results for sub-groups with no prior PTD.

The authors acknowledged limitations to their study. Specifically, the absence of indirect costs, the limited sources of effectiveness data, and the use of utility weights from a different population (low birth weight neonates) to that addressed (preterm births).

Implications of the study
The authors suggested that further studies are needed to confirm the assumption that utility weights obtained from the evaluation of low birth weight neonates are close approximations to those from preterm births, and to provide more reliable estimates of the costs.

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None stated.

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Other publications of related interest
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Indexing Status
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MeSH
Cost-Benefit Analysis; Decision Support Techniques; Female; Gestational Age; Health Care Costs; Hospitalization /economics; Humans; Hydroxyprogesterones /economics /therapeutic use; Multivariate Analysis; Obstetric Labor Complications /economics /epidemiology /prevention & control; Obstetric Labor, Premature /economics /epidemiology /prevention & control; Parity; Pregnancy; Premature Birth /economics /epidemiology /prevention & control; Progestins /economics /therapeutic use; Risk Factors; Secondary Prevention; United States

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