Cost-effectiveness of single-dose methotrexate compared with laparoscopic treatment of ectopic pregnancy

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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
Intramuscular (IM) methotrexate for small unruptured ectopic pregnancy.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of women with small unruptured ectopic pregnancies in the USA.

Setting
The setting was community. The economic study was carried out in Michigan, USA.

Dates to which data relate
The effectiveness evidence was derived from meta-analyses of studies conducted between 1980 and 1998. No date was provided for the estimate of resource use. Prices were from 1998.

Source of effectiveness data
Effectiveness data were derived from a review/synthesis of the literature.

Modelling
A decision-analytic computer model was used in order to synthesise the cost-effectiveness of the therapies under consideration.

Outcomes assessed in the review
The primary outcome was resolution of the ectopic pregnancy. The model also took account of complications associated with laparoscopy, as well as complications and side effects of methotrexate.

Study designs and other criteria for inclusion in the review
Results from studies of more than 30 cases were used to estimate resolution rates. Complication rates were estimated from all studies identified in the review, regardless of number of cases per study.
Sources searched to identify primary studies
The authors searched MEDLINE and references.

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

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Fourteen studies were used to derive the resolution rate for laparoscopy, whereas eight studies were used to derive the resolution rate for methotrexate. Twenty-three studies reported complication rates for the therapies.

Methods of combining primary studies
Resolution rates were estimated as simple and weighted averages, and complication rates were derived through use of simple averages.

Investigation of differences between primary studies
Not stated.

Results of the review
The results of the review were as follows:

The weighted average resolution rate was 91% (95% CI: 0.91 - 0.92) for laparoscopy.

The weighted average resolution rate was 72% (95% CI: 0.71 - 0.73) for single-dose methotrexate therapy and an additional 15% (95% CI: 0.15 - 0.16) when taking account of those patients to whom a second dose was administered (i.e., 87% for methotrexate therapy in total).

Complication rates were reported for different outcomes of the two different treatments. For laparoscopy, the risk of intraoperative complications was estimated at 2% and the risk of postoperative complications was estimated at 9% for both resolved and persistent pregnancies. In addition, the risk of haemodynamic instability for persistent pregnancies was estimated at 7%. For methotrexate therapy, the risk of minor complications was 10% and the risk of serious complications was 7% for both resolved and persistent pregnancies. In addition the risk of life-threatening complications was 14% for persistent pregnancies.

Measure of benefits used in the economic analysis
The measure of benefit in the economic analysis was the number of resolved ectopic pregnancies.

Direct costs
Resource costs and quantities were not reported separately, except as aggregates per care episode. Costs were not discounted as the short timeframe of the model made this irrelevant. Costs were estimated using cost-to-charge ratios at the US health care provider institution with which the authors were affiliated and were from 1998. Resource use associated with laparoscopy was estimated using the care protocol of the same institution that provided information on unit costs. Resource use associated with methotrexate was estimated using the protocol of a clinical trial. Costs for patients on methotrexate included six serum assays for Beta-hCG, one complete blood count and one follow-up visit. Costs for laparoscopy included the cost of using operating and recovery rooms, four Beta-hCG serum assays, one
complete blood count, five venipunctures and one follow-up visit. In addition, complication-related costs were estimated. Costs associated with diagnosis were assumed to be equal across treatments and were excluded. The total costs associated with each treatment strategy were estimated using a model.

**Statistical analysis of costs**
No statistical analysis of costs was reported.

**Indirect Costs**
Indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
A multi-way sensitivity analysis was used in order to present a worst-case scenario for variability in the data for methotrexate treatment. The model was evaluated using Monte Carlo simulation of a cohort of 10,000 patients to combine the costs of treatments and complications associated with treatments, with the benefits of treatment. The lowest estimate of resolution-rate and highest estimate of complication rates was used in combination with zero complication rates for laparoscopy and lowest estimate of laparoscopy costs.

**Estimated benefits used in the economic analysis**
Only percentages were reported (as in the Results of the review).

**Cost results**
The total intervention cost for laparoscopy as first line therapy was $4,100 and the total intervention costs for methotrexate therapy was $407 for single-dose treatment. For persistent pregnancies the additional cost of laparoscopy as second line treatment was $3,010 and the additional cost of a second dose of methotrexate therapy was $70. The cost of complications was included in the final estimate of average treatment costs.

**Synthesis of costs and benefits**
The model indicated a cost saving of $3,087 per resolved ectopic pregnancy with methotrexate treatment compared with laparoscopy (range: $1,385 - $3,239). Methotrexate therapy continued to be cost saving when using a series of ‘worst case scenario’ assumptions for methotrexate.

**Authors’ conclusions**
Methotrexate dominated laparoscopy even in the worst case scenario.

**CRD COMMENTARY - Selection of comparators**
Both methotrexate and outpatient laparoscopy are reported to be first-line therapies for ectopic pregnancy in the US by the authors of the paper, and are therefore relevant comparators for a US clinical setting.

**Validity of estimate of measure of effectiveness**
The measure of effectiveness was derived from studies identified in a MEDLINE search, and may therefore have been based on a comprehensive review. The search strategy was, however, not reported, and lack of explicit inclusion criteria and quality standards for the studies combined with lack of detail in description of statistical methods by which the
probabilities of clinical events were combined, may raise doubt about the validity of the measure of effectiveness.

**Validity of estimate of measure of benefit**
Please refer to the comments on measure of effectiveness, given that there was no summary measure of benefit.

**Validity of estimate of costs**
The charges used to cost resource use were derived in the US health care setting and may not be relevant to other settings. Assumed resource use was reported separately from unit costs, but only as aggregate costs for an episode of treatment were provided in the paper. The ability to assess whether the cost-estimates are relevant in other settings is therefore limited.

**Other issues**
Comparison was made with other studies and the issue generalisability, given cost and effectiveness issues particular to an institution, was discussed. The authors do not appear to have presented the results selectively and their conclusions seem to reflect the population concerned, although information on baseline characteristics might have been useful.

**Implications of the study**
The authors stated that their study supports the use of methotrexate as front-line therapy for small unruptured ectopic pregnancy, but acknowledged that acceptable resolution rates with this therapy may only be achieved in clinical environments that support the effective use of the intervention.

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