**Cost-effectiveness of presumptively medically treating women at risk for ectopic pregnancy compared with first performing a dilatation and curettage**

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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**
Two alternative strategies for the diagnosis and medical treatment of ectopic pregnancy when ultrasound is nondiagnostic were examined. Dilatation and curettage (D&C) followed by treatment of all ectopic pregnancies with methotrexate (MTX) was compared with the empiric treatment of all patients with possible ectopic pregnancies with MTX without D&C. Single- and multi-dose MTX treatments were evaluated for nonviable pregnancies. Two definitions of nonviable pregnancies (with different ectopic pregnancy risks) were evaluated. One definition was a pregnancy with a human chorionic gonadotropin (hCG) level greater than 2,000 mIU/mL, and no evidence of intrauterine pregnancy on ultrasound. The other definition was a pregnancy with an hCG level less than 2,000 mIU/mL which was not rising appropriately.

**Type of intervention**
Diagnosis and treatment.

**Economic study type**
Cost-effectiveness analysis.

**Study population**
The hypothetical population was a cohort of 10,000 women with nonviable pregnancies and a known incidence of ectopic pregnancy.

**Setting**
The setting was tertiary care. The economic study was carried out at the University of Pennsylvania Medical Centre, USA.

**Dates to which data relate**
The effectiveness evidence dated from 1979 to 2003. The cost data were from 1992. The price year was not reported.

**Source of effectiveness data**
The evidence was derived from a review or synthesis of completed studies, along with estimates based on published literature and authors' assumptions.

**Modelling**
A decision analysis was carried out using decision tree designed to compare strategies. The decision analysis was performed for single- and multi-dose MTX.
Outcomes assessed in the review
The parameters used in the model included:

missed ectopic pregnancies and spontaneous abortions (SAB),

D&C complications,

the sensitivity and specificity of frozen section,

MTX overall side effects,

MTX treatment success rate, and

fallopian tube rupture rates.

Failed treatment of ectopic pregnancies was also evaluated. The necessity of a second treatment and complications were also included.

Study designs and other criteria for inclusion in the review
Randomised clinical trials and other studies of varied designs were considered. No inclusion or exclusion criteria were reported.

Sources searched to identify primary studies
MEDLINE was searched using the keywords "ectopic pregnancy, D&C, and methotrexate".

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
Thirteen primary studies were included in the review.

Methods of combining primary studies
A narrative method was used to combine the studies.

Investigation of differences between primary studies
Not reported.

Results of the review
The parameters used in the model for the base-case were as follows.

The D&C complication rate was 3%.

For the efficacy of frozen section, the true ectopic pregnancy was 98.4%, false positive, 7.4%, true negative (true SAB) 78.3% and false negative 1.6%.
The rate of MTX side effects was 31.3% for a single dose and 41.2% for multiple doses.

The success rate was 88.1% for a single dose and 92.7% for multiple doses.

The rupture rate was 75% for those treated with single-dose MTX and multi-dose MTX, and 18% for those untreated (missed ectopic pregnancy).

The success rate of SABs treated with MTX was 80%.

**Methods used to derive estimates of effectiveness**
The study was based on published data and authors’ assumptions.

**Estimates of effectiveness and key assumptions**
A nonviable pregnancy was defined as either a pregnancy with an hCG level greater than 2,000 mIU/mL and no evidence of intrauterine pregnancy on ultrasound, or a pregnancy with an hCG level less than 2,000 mIU/mL which was not rising appropriately. An ectopic pregnancy falsely diagnosed as a miscarriage was considered an unsuccessfully treated ectopic pregnancy in the model.

**Measure of benefits used in the economic analysis**
The major outcome measure from the model was the percentage of successful treatments of ectopic pregnancy. The percentage of cases with complications was also derived.

**Direct costs**
The resources used were D&C, MTX doses, complications from D&C, complications from receiving MTX, hospitalisations and endoscopies. The costs were presented as an average per patient in each group. The costs for each medical procedure were calculated from the relative resource value units from the Centre for Medicare Statistics, using a factor conversion of $36.1992 per resource value unit. Discounting was not carried out since the costs were incurred during less than 2 years. The quantities and the costs were not analysed separately. Estimations of the quantities and costs were derived by modelling. The price year was not reported.

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

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

**Currency**
US dollars ($).

**Sensitivity analysis**
The uncertainty of the results was assessed through one-way sensitivity analyses, performed using values from published literature. The analyses required the number of women experiencing each of the outcomes and complications to be recalculated after changing the value of one outcome probability variable. A priori, the model was considered sensitive to any outcome probability that resulted in a 15% change in primary outcomes.

**Estimated benefits used in the economic analysis**
For the model with single-dose MTX and no intrauterine pregnancy, the proportion of successes was 87.1% for D&C and 88.1% for MTX.

For the model with single-dose MTX and plateau hCG, the proportion of successes was 87.8% for D&C and 88.1% for MTX.

For the model with multi-dose MTX and no intrauterine pregnancy, the proportion of successes was 91.7% for D&C and 92.7% for MTX.

For the model with multi-dose MTX and plateau hCG, the proportion of successes was 92.4% for D&C and 92.7% for MTX.

**Cost results**

In the single-dose MTX treatment model, for the no intrauterine pregnancy group, the average cost per patient was $389 for D&C and $216 for MTX. For the plateau hCG group, the costs were $444 for D&C and $223 for MTX.

In the multi-dose MTX treatment model, for the no intrauterine pregnancy group, the average cost per patient was $373 for D&C and $198 for MTX. For the plateau hCG group, the costs were $420 for D&C and $197 for MTX.

D&C cost $173 to $223 per patient more than the empiric use of MTX.

**Synthesis of costs and benefits**

Not relevant.

**Authors’ conclusions**

The results demonstrated a remarkable equivalence of both treatment strategies in terms of treatment success, number of side effects and cost. In other words, these data did not support any objective superiority of presumptively treating a woman with methotrexate (MTX) at risk for an ectopic pregnancy, with a nonviable pregnancy of unknown location, compared with first performing a dilatation and curettage (D&C). In addition, there was a mild cost-difference of approximately $200 between these two strategies, which is usually considered non significant when comparing two competing strategies.

**CRD COMMENTARY - Selection of comparators**

The authors gave a justification for the comparators. To date, no clinical trial has evaluated the optimal treatment of women at risk for ectopic pregnancy, especially those with a nonviable pregnancy of unknown location. Also, the presumptive medical treatment might prevent both the complications and the expense of a D&C, but because a definitive diagnosis would not be made, this practice would unnecessarily treat some women with an abnormal intrauterine pregnancy with MTX. You should judge whether these strategies are relevant in your setting, or whether other comparators from other drugs and treatments could also be relevant.

**Validity of estimate of measure of effectiveness**

The authors did not state that a systematic review of the literature had been undertaken. Although this is a common practice with models, it does not always ensure that the best data available are used in the model. The authors used data from the available studies selectively. One cannot be sure that all the relevant literature was identified, although it is certain that randomised clinical trials were used to derive the effectiveness and complications, and that few authors’ assumptions were made. The estimates of effectiveness were derived credibly from the studies identified. The authors used data from published sources and their own assumptions. The sources of effectiveness evidence were derived from clinical trials, which are an adequate source to estimate effectiveness. The authors justified their assumptions with reference to the medical literature. The estimates were investigated in sensitivity analyses using ranges from the literature, but the authors did not justify the ranges selected and reported.
Validity of estimate of measure of benefit
The model produced more than one outcome measure. The main measure was the percentage of successful treatments of ectopic pregnancies. This is a useful clinical outcome but it does not lend itself to economic comparisons with interventions in other disease areas. The appropriate economic measure is the cost per unit of health outcome.

Validity of estimate of costs
The perspective of the study was not reported. The authors acknowledged that the costs reported in the paper were health care charges taken from published sources. The cost of time related to treatment for the health care provider or patient was not included in the analysis. MTX for all patients would be likely to decrease physician time, but actually increase the "collective" treatment time for women with a nonviable pregnancy and the time of medical support staff. No statistical analysis of the costs was undertaken. Sensitivity analyses of the direct costs were not reported. Discounting was appropriately not carried out since the time horizon did not exceed 2 years. The price year was not reported, which will hinder any future reflation exercises.

Other issues
The authors did not make appropriate comparisons of their findings with those from other studies. They explicitly addressed the generalisability of the results by considering that different patient populations might prefer one treatment strategy over the other, depending on informed consent and expectations. The authors conclusions reflect the scope of the analysis. The authors stated that some limitations of the model were related to factors which are difficult to quantify in a decision analysis. For example, the lack of a diagnosis, future fertility effects, the chance of subsequent ectopic pregnancies, the emotional ramifications of giving MTX to patients unnecessarily, and the possibility of giving a possible abortifacient or teratogenic agent to a normal pregnancy.

Implications of the study
The parameters used in the model, including incidence of ectopic pregnancies and the accuracy of frozen section, might differ greatly between different populations, hospitals and providers. In addition, the authors stated that they were unable to quantify the severity of side effects and to understand how these side effects would be perceived. Therefore, in certain clinical situations one approach might be clearly preferable to the other. Different patient populations might prefer one treatment strategy over the other depending on informed consent and expectations. Some other factors that could affect medical decision-making for patients and clinicians are difficult to quantify in a decision analysis. These factors favour the use of D&C to rule out miscarriage before treatment with MTX. Perhaps in the future, less invasive means of eliminating the possibility of a miscarriage, such as menstrual extraction or novel noninvasive techniques to diagnose an ectopic pregnancy, might prove beneficial to this clinical problem.

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