Economic evaluation of alternative management methods of first-trimester miscarriage based on results from the MIST trial

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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 authors compared expectant, medical and surgical treatment of first-trimester miscarriage. Medical treatment for incomplete miscarriage comprised a single vaginal dose of 800 microgram misoprostol, while for missed miscarriage it comprised a single oral dose of 800 microgram misoprostol 24 to 48 hours later. Surgical treatment was the surgical evacuation of the retained products of conception. Expectant management consisted of doing nothing (no intervention).

Type of intervention
Secondary prevention of infection.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women with a confirmed pregnancy of less than 13 weeks' gestation with a diagnosis of incomplete miscarriage or missed miscarriage.

Setting
The setting was secondary care (early pregnancy assessment units). The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data referred to May 1997 to December 2001. The price year was 2001/02.

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

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The authors clearly stated that details of the effectiveness study had been reported elsewhere (Trinder et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). The authors reported that women with a confirmed pregnancy of less than 13 weeks’ gestation with a diagnosis through transvaginal scan of incomplete miscarriage or missed miscarriage/early foetal demise were included in the study. Women were recruited from seven early pregnancy assessment units in southern England. There was no report that power calculations were carried out to estimate the impact of chance on the results. A total of 1,200 women entered the study, of which 399 were allocated to
receive expectant management, 398 to receive medical treatment and 403 to receive surgery.

**Study design**

The authors designed a randomised controlled trial with participants being randomised by telephone. The participants were observed over a follow-up period divided into the first 14 days and the first 8 weeks post-randomisation. The authors did not report any loss to follow-up. Blinding of the patients was not possible, although it might have been possible to blind those involved in data collection; there was no report that this was carried out.

**Analysis of effectiveness**

The analysis of the results was based on intention to treat principles. The primary health outcome was documented gynaecological infection, defined as two or more of purulent vaginal discharge, pyrexia > 38.0 degrees C, tenderness over the uterus on abdominal examination, and/or increase in white cell count above 15 x10^9/mL. While the authors did not report the comparability of the groups, this information might have been given in the parent study.

**Effectiveness results**

The authors reported that there were no significant differences between the three groups in terms of incidence of gynaecological infection within the first 14 days or within the first 8 weeks following randomisation. However, these results were not shown in the present paper.

**Clinical conclusions**

The three forms of treatment were found to be equally effective.

**Measure of benefits used in the economic analysis**

As the effectiveness analysis demonstrated equal effectiveness for the two treatment options, the economic analysis should have been characterised as a cost-minimisation analysis. However, the authors used the number of gynaecological infections avoided as the summary measure of health benefit and calculated incremental cost-effectiveness ratios (ICERs).

**Direct costs**

The costing was carried out from a societal perspective. It encompassed the cost to the hospital and community health and social services, and costs borne by the affected women and their informal carers. For each woman participating in the study, data collection forms collated resource use data such as duration and frequency of hospital admissions, consultations, emergency admissions, type and quantity of analgesia, data on intravenous infusions, and duration of surgery. In addition, health care staff recorded contacts with each patient, providing information about the type and grade of the health care professional attending, the number of contacts and the duration of contacts. Postal questionnaires were completed by the women to record number, type and duration of community health care contacts made, as well as personal costs such as child care support and travel costs. The unit costs were based on institution-specific data, published sources, national sources and estimates provided by the women involved. The unit costs and resource use were reported separately. Discounting was not required given the relatively short time horizon of 8 weeks. The price year was 2001/02.

**Statistical analysis of costs**

The authors estimated 95% confidence intervals (CIs) and tested for differences between groups using independent t-tests. The authors set a significance level of 0.05 or less. Non-parametric bootstrapping was used to identify CIs for the skewed cost data and this involved 1,000 bias-corrected replications. Statistical methods were used to account for information that was considered to be censored.
Indirect Costs
In accordance with the stated perspective of the study, the authors estimated the costs of lost production by asking women how long they had to be off work as a consequence of the miscarriage. Absences were valued using gender-specific median salaries provided by a national published source.

Currency
UK pounds sterling (£).

Sensitivity analysis
The authors used one-way sensitivity analyses to explore the implications of uncertainty surrounding the base-case ICERs. The authors explored the impact of community service use, the per diem costs for each level of gynaecological care, the mean level of medical and nursing staff support, and the economic value of each day of work absence. Although ranges were stated it was unclear how these were agreed.

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

Cost results
The net social costs per woman were 1,086.2 in the expectant group, 1,410.4 in the medical group and 1,585.3 in the surgical group.

The authors noted that this represented savings of 324.2 (bootstrap mean difference 321.4, 95% CI: 197.0 to 435.4; p<0.001) and 499.1 (bootstrap mean difference 496.7, 95% CI: 385.0 to 603.4; p<0.001) when expectant management was compared with medical and surgical treatment, respectively.

There was a saving of 174.9 (bootstrap mean difference 175.3, 95% CI: 79.1 to 268.9; p<0.001) when medical treatment was compared with surgery.

Synthesis of costs and benefits
When compared with surgery, the cost per gynaecological infection avoided was -204,968.9 for expectant management and -26,258.4 for medical treatment.

When compared with expectant management, the cost per gynaecological infection avoided for surgery was 63,096.8.

Cost-effectiveness acceptability curves showed that expectant management had a 97.8% probability of being the most cost-effectiveness strategy, and medical treatment a 2.2% probability at a willingness-to-pay threshold of 10,000.

The authors noted that expectant management retained the highest probability of being cost-effective at all thresholds of less than 70,000 for preventing one gynaecological infection.

Sensitivity analyses revealed that the ICER was not sensitive to the number of community service contacts reported, the mean level of medical and nursing staff support, or the economic value of each day of work absence. The results were sensitive to the per diem costs for each level of gynaecological care.

Authors’ conclusions
The authors concluded that their study demonstrated "the economic advantages of expectant and medical management of first-trimester miscarriage in comparison to surgical management".
CRD COMMENTARY - Selection of comparators
The authors compared expectant, medical and surgical treatment of miscarriage. These alternatives represented each of the possible alternatives available in any clinical setting and so are widely applicable.

Validity of estimate of measure of effectiveness
The randomised controlled nature of the study was an appropriate design in terms of reducing potential systematic differences between women in the two groups, and increasing the validity of the results. The study would have benefited from a written report of the comparability between the groups which explored, for instance, the number of missed and incomplete miscarriages in each group. Such a comparison would help the reader understand any differences between the two groups that might act as confounding variables. This information may have been available in the parent study. The results were analysed by intention to treat in order to control for the influence of any women changing treatment during the trial. However, the effectiveness results were not reported in detail in the present paper, and only the conclusions drawn from the previous paper were reported.

Validity of estimate of measure of benefit
Although no statistically significant difference was found between the three groups and, therefore, the authors’ conclusions were that “the three forms of management were found to be equally effective”, the number of gynaecological infections avoided was used as the summary measure of health benefit. This outcome measure is very situation specific and would prevent comparisons of outcome beyond the immediate clinical setting. The authors noted that the use of a broader economic variable might assist the understanding of women's preferences such as the location of their care.

Validity of estimate of costs
The authors adopted a societal perspective and included cost elements that were relevant to this. They gave a thorough description of their costing analysis, reporting the price year and separating the extensive reporting of unit costs and resource usage. The impact of uncertainty on the results was explored using sensitivity analysis, as well as tests of statistical difference, bootstrapping and cost-effectiveness acceptability curves. The results were presented as ICERs, which permit a comparison of the relative benefits of each available technology. The analysis could have been improved by the inclusion of a temporal profile of when the costs were incurred, as the reader might naturally assume that the majority of costs were incurred soon after randomisation, but that some costs were incurred later. As a potential limitation of the study, the authors acknowledged the possibility that some costs might have been omitted because of the short timeframe.

Other issues
The authors did not make comparisons with any previous studies. However, it was unclear whether this was the first study of this nature, which would mean that comparisons might not be possible. The issue of generalisability to other settings was considered and the authors invited readers to explore this factor. Generalisability was improved by the extensive statistical and sensitivity analyses. The authors’ conclusions were an accurate reflection of the results presented, although they may have reiterated the non statistical difference in outcomes more strongly. Several limitations were discussed. These focused on the fact that the outcomes data were based on this single trial, the limited time horizon, not using a preference-based measure of outcome, and not adopting a broad economic approach to outcome valuation that enables monetary values to be placed on the outcomes.

Implications of the study
The authors noted that it is for policy-makers to interpret the results of this study within their own setting and make recommendations for policy.

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Other publications of related interest
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