Cost-effective treatment of women with advanced ovarian cancer by cytoreductive surgery and chemotherapy directed by an in vitro assay for drug resistance

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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 use of cytoreductive surgery, followed by chemotherapy directed by an in vitro assay for drug resistance. Women with advanced ovarian cancer were given surgery (including hysterectomy, bilateral salpingoophorectomy and removal of the omentum) that was designed to achieve maximal cytoreduction. Fourteen to 28 days after the surgery the women were given 6 courses of chemotherapy, except in cases of progression. The chemotherapy used for each patient depended partly on the results of testing malignant tissue obtained from surgery for its resistance to different drugs. The tissue was tested for resistance to paclitaxel, cyclophosphamide, carboplatin and cisplatin. The testing procedures have been described elsewhere (see Other Publications of Related Interest).

The doses planned for chemotherapy were cisplatin 100 mg/m2, carboplatin 300 mg/m2, cyclophosphamide 600 mg/m2 and paclitaxel 135 mg/m2. However, these were later altered to take account of white blood cell and platelet counts.

The chemotherapy consisted of either paclitaxel plus platinum (TP) or cyclophosphamide plus platinum (CP).

An algorithm was followed to decide whether TP or CP was given to the patients. The rules of the algorithm took account of the drug resistance that had been identified. The 'platinum' given was cisplatin. If cisplatin could not be tolerated then carboplatin was given.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women with advanced ovarian cancer. The inclusion criteria were histological confirmation of epithelial ovarian cancer, International Federation of Gynecology and Obstetrics (FIGO) stage III, no prior chemotherapy or radiation, no coexisting neoplasm, and optimal residual disease (less than 2 cm).

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

Dates to which data relate
The effectiveness evidence was gathered from January 1992 to April 1995. The dates during which the resources use data were obtained were not given. The price year was not given.
Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out on the same patient sample as that used for the effectiveness data. However, it was unclear whether the costing was conducted prospectively or retrospectively.

Study sample
No power calculations to determine the sample size were carried out. All patients satisfying the inclusion criteria, and who attended the cancer centre during the time period described above, received treatment according to the protocol in which the in vitro drug assay influenced the choice of chemotherapy. The patients were not asked to consent to the in vitro testing of malignant tissue. Sixty-six patients were treated according to the protocol. There were 47 patients in the TP group and 19 in the CP group.

Study design
This was a non-randomised study, in that patients were allocated to either TP or CP following in vitro assessment. The authors assessed the consequences of treatment after the in vitro assay for drug resistance, but they did not have a comparator group against which to compare the overall results. The study was carried out in a single centre with a median follow-up of 24 months. No loss to follow-up was reported.

Analysis of effectiveness
The analysis was conducted on an intention to treat basis. The primary health outcome used was the 3-year survival rate. The authors aimed to evaluate the effect of the in vitro assay, but they did not have a control group of patients without an in vitro assay.

Effectiveness results
The 3-year survival rate for the 66 patients was reported as 68% (95% confidence interval, CI: 47 - 79) in the legend of Figure 2. However, in the text, the 3-year survival rate was given as 69% (95% CI: 58 - 80). The patients in the TP group (n=19) had a 3-year survival of 66%, whilst those in the CP group (n=47) had a 3-year survival of 74%.

Clinical conclusions
The authors showed that using in vitro assays for drug resistance was practical in treating women with ovarian cancer. Their results appeared to be good in comparison with other studies. The 3-year survival was similar for TP and CP groups. However, the authors did not compare their results with those obtained from women in exactly the same medical condition, who were receiving chemotherapy without in vitro assays for drug resistance.

Modelling
The Kaplan-Meier method was used to estimate the 3-year survival rate.

Measure of benefits used in the economic analysis
The measure of benefit was the percentage of women who survived for three years. The cost per life-year saved was also calculated from the survival rates.

Direct costs
The quantities and the costs were not analysed separately. No discounting was carried out, and there was no evidence that adjustment to a common price year was made. The costs were estimated from actual data. The costs were
calculated for chemotherapy and the in vitro assays. The price of drugs was taken as the median average wholesale price, although the source was not given. The price year was not given.

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

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
The costs of chemotherapy were calculated assuming a discount of 25% from the average wholesale price.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section. The side-effects of treatment were not considered. The cost to save one life-year is reported in the 'Synthesis of Costs and Benefits' section.

**Cost results**
The average cost of chemotherapy per patient, excluding the cost of the in vitro assay, was $5,850.

**Synthesis of costs and benefits**
The cost of treatment ($6,740) and the 3-year survival rate of 69% were combined to produce a figure of $9,768, representing the cost of a life-year saved.

**Authors’ conclusions**
The authors concluded that the 3-year survival rates for their patients were good when using the health technology under assessment. They also concluded that the cyclophosphamide-platinum (CP) and paclitaxel-platinum (TP) groups of patients had similar 3-year survival rates. The cost-effectiveness results were similar to those of other studies examining TP.

**CRD COMMENTARY - Selection of comparators**
There was not a valid selection of the comparator in terms of the in vitro elements of this study. The authors examined the consequences of an in vitro assay for drug resistance followed by chemotherapy using two appropriate regimens (TP and CP).

**Validity of estimate of measure of effectiveness**
The study design was inappropriate for the hypothesis. The study ought to have compared two groups of patients, one receiving chemotherapy modified by an in vitro assay for drug resistance and the other receiving chemotherapy without the use of this assay. The comparisons of CP and TP were based on a non-randomised selection process which, as the authors acknowledged, leads to a susceptibility to bias and confounding variables. Thus, the results need to be treated with some caution.
Validity of estimate of measure of benefit
The authors used an estimate of benefit derived directly from the effectiveness estimate, the 3-year survival rate. However, it would have been useful to know the extra years gained as a result of using the in vitro assay in comparison with standard practice.

Validity of estimate of costs
The study design had some limitations in terms of the measurement of costs, which were confined to the drug costs only. The authors reported another study that recorded the cost of toxicity monitoring for paclitaxel therapy, indicating an example of the type of cost which could have been included in a study comparing patients with and without in vitro assay. The costs, quantities and prices were not reported separately, which limits their generalisability to other settings. The price year and the sources used were not specified, making reflation exercises in other settings problematic.

Other issues
The authors made comparisons of their results with those from other studies. However, the issue of generalisability was not addressed. The authors' conclusions reflect the scope of the analysis, which, as the authors acknowledge, would need more rigour in future research.

Implications of the study
The authors' findings are informative and suggest benefits can be gained using in vitro-guided techniques. However, there should be a randomised controlled trial to assess the benefits and the costs of in vitro assays. Such a trial should include the side-effects of drugs in the benefits and should give comprehensive information on the costs.

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Other publications of related interest


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