Centralization of care for patients with advanced-stage ovarian cancer: a cost-effectiveness analysis


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 compared two different referral strategies for patients with advanced-stage ovarian cancer. One strategy was referral to an expert centre, with a rate of optimal primary cytoreduction of 75% and use of combined intraperitoneal and intravenous adjuvant chemotherapy. The other strategy was referral to a less experienced centre, with a rate of optimal primary cytoreduction of 25% and adjuvant treatment consisting predominantly of intravenous chemotherapy alone.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of women with advanced-stage ovarian cancer.

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

Dates to which data relate
The effectiveness data were derived from studies published between 1983 and 2006. The costs were derived from data derived between 2004 and 2006. The price year was 2006.

Source of effectiveness data
The effectiveness data included in the model were:

- the rate of optimal primary cytoreduction;
- the rate of complete cytoreduction;
- the proportion of patients receiving intraperitoneal (IP)/intravenous (IV) chemotherapy; and
- the operative mortality of primary surgery.

The clinical data included in the model were:

- survival data associated with IP/IV (IP cisplatin plus IP and IV paclitaxel) and IV/IV (IV carboplatin plus IV paclitaxel) chemotherapy; and
the incidence of hospitalisation for fever, infection, gastrointestinal toxicity, metabolic events, thrombocytopenia and renal or genitourinary events.

**Modelling**
A decision analytic tree model was generated to evaluate the two management practices, for patients with advanced-stage epithelial ovarian cancer, from primary cytoreductive surgery through to the completion of front-line chemotherapy. The details of the model were presented in full.

**Sources searched to identify primary studies**
The authors reported that, whenever possible, data from Phase III trials were utilised. However, when such data were unavailable, data for the model parameters were derived from Phase II trials, case-control studies, retrospective case series and expert opinion. The authors also reported that all survival estimates were generated from the actual or projected median survival from Phase III trials of patients with advanced-stage ovarian cancer.

**Methods used to judge relevance and validity, and for extracting data**
The authors reported that they conducted a review of literature published in the English language to obtain data for the model parameters. However, they did not report further methods of this review nor how the results from different studies were combined. In addition, they did not provide any details on how expert opinion was elicited or the experts consulted.

**Measure of benefits used in the economic analysis**
The measure of benefits used was the quality-adjusted life-years (QALYs) gained. Utility values associated with the toxicity of chemotherapy during the first year of survival were estimated from longitudinal quality of life assessments using the Functional Assessment of Cancer Treatment - Oncology. Discounting was relevant, as the benefits could be incurred over the lifetime of the patient, and was appropriately performed at an annual rate of 3%.

**Direct costs**
The direct costs included in the analysis were those to the health care system. These included the costs of primary surgery, the costs associated with the IP and IV chemotherapy regimens, and the hospitalisation costs for treatment-related toxicity. The costs of primary surgery were derived from medical charges based on the index admission of 40 consecutive patients undergoing primary cytoreductive surgery. The costs of the IP chemotherapy regimen were based on a reported protocol used in another study and costed using hospitalisation reimbursement rates. The costs of the IV chemotherapy regimen were based on mean hospital charges. The costs of hospitalisation due to chemotherapy toxicity were derived from a review of Maryland patients who were admitted during 2005 and 2006. The costs appear to have been incurred during less than 1 year, consequently discounting was not relevant. The price year was 2006. The authors reported the average costs.

**Statistical analysis of costs**
The costs were treated as point estimates (i.e. the data were deterministic).

**Indirect Costs**
The productivity costs associated with loss of work due to disease morbidity and caregiver support were included in the analysis. Productivity costs due to loss of work were estimated for a 6-week period during surgery, plus an additional 16 weeks to complete the treatment programme. These were then valued using average hourly earnings, after adjustment for employment-to-population ratios. Caregiver support costs were calculated by assuming care was given during the postoperative recovery period and during treatment cycles. The productivity costs appear to have been incurred during less than one year, consequently discounting was not relevant. The price year was 2006.
Currency
US dollars ($).

Sensitivity analysis
The authors performed a series of one-way sensitivity analyses for each of the model parameters. A tornado diagram was then developed to show the impact of variations in each model parameter on final cost-effectiveness. Probabilistic sensitivity analyses were also performed using Monte Carlo simulation with 10,000 samples. The authors assumed a triangular distribution for all the model parameters.

Estimated benefits used in the economic analysis
When survival time was undiscounted, the QALYs gained were 2.33 for the less experienced centre and 5.12 for the expert centre.

With discounted survival time, QALYs gained were 2.14 for the less experienced centre and 4.24 for the expert centre.

Cost results
When survival time was not discounted, the costs incurred by each patient were $39,957 for those attending the less experienced centre and $50,652 for those attending the expert centre.

When survival time was discounted, the costs incurred by each patient were $40,116 for those attending the less experienced centre and $50,592 for those attending the expert centre.

It would appear that the costs themselves were not discounted.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-utility ratio (i.e. the additional cost per QALY gained when referral to an expert centre was compared with referral to a less experienced centre). When the benefits were not discounted, the incremental cost-utility ratio was $3,809 per QALY gained, whereas when the benefits were discounted, the incremental cost-utility ratio was $5,029 per QALY gained.

Results of the sensitivity analysis showed that the costs of IV/IV and IV/IP chemotherapy together with the probability of IP/IV chemotherapy at the less experienced centre were the factors that were most likely to affect the cost-effectiveness results. The results of the 10,000 samples in the Monte Carlo analysis showed that the expert centre was consistently more effective than the less experienced centre, whereas the costs of the two centres did not differ significantly. The mean cost was $40,479 (95% confidence interval, CI: 32,343 to 48,627) for the less experienced centre and $50,638 (95% CI: 40,384 to 62,100) for the expert centre.

Authors' conclusions
The referral of patients with ovarian cancer to an expert centre was a cost-effective health care strategy.

CRD COMMENTARY - Selection of comparators
No justification was given for using a referral strategy to a less experienced centre as the comparator. However, this strategy would appear to represent current practice in the authors' settings. You should decide if the comparator used represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The parameters were derived from published research and expert opinion. The authors did not report whether data from different studies were combined and did not report the methods used. The authors reported that, whenever possible, data from Phase III trials were utilised, with other types of data being used when these were unavailable. However, they
did not mention any search methods or any inclusion criteria. They also did not report on how expert opinion was elicited.

**Validity of estimate of measure of benefit**
The estimation of health benefit (i.e. QALYs gained) was derived appropriately using a decision analytic tree model. The QALYs gained were appropriately discounted. The utilities used to form QALYs were derived from longitudinal quality of life assessments.

**Validity of estimate of costs**
The analysis of the costs was performed from a societal perspective. All the relevant categories of costs appear to have been included in the analysis. However, in the productivity costs, the authors did not include the costs associated with early mortality. Consequently, the model would appear to bias against referral to an expert centre, which was associated with higher life expectancy. The costs were derived from published sources, with charges being used to proxy prices. However, these were later converted into costs using cost-to-charge ratios. It would appear that the costs were only incurred during a period of less than 1 year. For this time horizon, discounting was not relevant. The authors evaluated uncertainty in the cost data jointly with the effectiveness data by performing a Monte Carlo simulation with 10,000 samples to produce a confidence ellipse showing the estimated costs and benefits. The price year was reported, which will ease any future inflation exercises.

**Other issues**
The authors reported that population-based studies had shown that high-volume or expert centres were associated with superior outcomes to low-volume centres for patients with ovarian cancer. The issue of generalisability to other settings was addressed in the authors' thorough sensitivity analyses. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported a number of further limitations to their study. First, the hypothetical nature of the model required a series of assumptions. Second, survival data were derived from only two studies. Third, median (rather than mean) survival times were used; this assumes a normal distribution and does not take irregularities in survival curves into account. Finally, the estimates were generated from a single institution, hence limiting the generalisability of the results.

**Implications of the study**
The authors reported that their data point out prime opportunities to improve the health care delivery system for women with suspected advanced ovarian cancer.

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**Other publications of related interest**
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