Reducing ovarian cancer mortality through screening: is it possible, and can we afford it?
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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.

CRD summary
The aim was to investigate the impact of possible ovarian cancer screening strategies, with various screening intervals, test characteristics, and costs. The strategies included no screening and screening at intervals of 3 to 36 months. The authors concluded that annual screening had the potential to be cost-effective, particularly in high-risk populations, and it achieved clinically acceptable positive predictive values if the test specificity exceeded 99%. The authors’ conclusions appear to be appropriate for the scope of their study.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study evaluated the clinical impact and cost-effectiveness of potential screening strategies for ovarian cancer.

Interventions
The aim was not to evaluate an existing test, but to investigate the impact of possible strategies with various screening intervals, test characteristics, and costs. The strategies included no screening and screening at intervals of 3 to 36 months.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A Markov model representing the natural history of ovarian cancer was constructed. Patients entered the model at age 20 years and screening commenced between the ages of 50 and 85 years. Extensive model details and assumptions were reported and two alternative risk scenarios were simulated. The time horizon was lifetime and the authors stated that the perspective of the health care system was adopted.

Effectiveness data:
Age-associated ovarian cancer incidence and staging data were obtained from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database. The analysis used an imputation process to estimate clinically reasonable values for some transition probabilities that were not available. The age-specific rates for hysterectomy, benign oophorectomy, and removal of both ovaries, were derived from the literature. The base-case sensitivity and specificity of the screening test were taken from two recent biomarker studies. Several assumptions were made relating to the disease progression in order to facilitate modelling. The main clinical parameters included the sensitivity and specificity of screening, probability of oophorectomy prior to age 20 years, five-year survival for different stages (I, II, III, and IV) of cancer, and mortality.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The years of life saved were the benefit measure. Other measures were reduction in mortality, lifetime number of false-positive screening tests, and positive predictive value. The years of life saved were discounted at an annual rate of 3%.
Cost data:
The direct costs included the costs of screening, procedures, and additional treatment. The unit costs were presented and were based on a national reimbursement database (Medicare) and practice guidelines. The cost of the screening test was based on authors' assumptions. The resource use estimates were based on both the literature and authors' assumptions. Future costs were discounted at an annual rate of 3% and all costs were in US dollars ($) for the year 2007.

Analysis of uncertainty:
Extensive one-way sensitivity analysis was conducted on all the model inputs using published ranges for clinically valid parameters. The ranges of costs were based on authors' assumptions, but they were wide ranges.

Results
In a population of unscreened women from age 20 to 100 years, the model predicted the lifetime risk of ovarian cancer to be 1.38% and death to be 0.95%. It predicted the stage distribution in the unscreened population as 19% at stage I, 7% at stage II and 74% at stage III, IV, or unstaged. Extensive model results were reported, but mainly the base case is presented here.

Annual screening from age 50 to 85 years was associated with a reduction in ovarian cancer mortality of 43%. This mortality reduction improved by approx 1% for every 5% increase in test sensitivity. The annual screening generated a positive predictive value of 0.55% and an average lifetime false-positive screening tests of 1.06.

For women aged between 50 and 85 years, annual screening generated 0.0080 life-years gained at an additional cost of $589 per person, resulting in an incremental cost-effectiveness ratio (ICER) of $73,469 per year of life saved compared with no screening. The ICER was $36,025 per year of life saved for high-risk women.

Increasing the test specificity to 99.9% improved the positive predictive value of annual screening to 22%. At a specificity of 99%, the positive predictive value of screening never exceeded 4% regardless of the screening frequency.

The deterministic one-way sensitivity analysis showed that the ICER was sensitive to the cost of the test, its performance characteristics, and the screening interval. The results of the sensitivity analysis were fully reported.

Authors' conclusions
The authors concluded that annual screening had the potential to be cost-effective, particularly in high-risk populations, and achieved clinically acceptable positive predictive values if the specificity exceeded 99%.

CRD commentary
Interventions:
The model compared a full range of potential screening strategies, all of which utilised the same test, but over different screening intervals, with different test characteristics, and at different costs. All the potential screening strategies were compared with no screening. The details of the potential strategies were well reported.

Effectiveness/benefits:
The authors appear to have selected what they believed to be the relevant sources of data. The SEER database was well established and a good source for cancer data. The authors also used clinical studies, but few details were reported for these, which makes it impossible to judge the validity of the clinical inputs. The derivation of the benefit measure was based on the modelling framework. Life-years are a validated benefit measure and permit cross-disease comparisons.

Costs:
The economic analysis was appropriately performed and the costs and resources included were consistent with the perspective. The unit costs were reported only for the screening test. The disease costs were reported as macro-categories due to the use of diagnosis-related group data. Other details of the study such as the price year, sources of costs, and discounting, were reported. Overall, the level of reporting around the cost inputs and adjustments was good.

Analysis and results:
The model structure, inputs, and assumptions were all well presented. The synthesis of the costs and benefits was based on an incremental approach, which was well conducted and adequately reported. The issue of uncertainty was addressed in extensive sensitivity analysis, but this was all one-way and not probabilistic, which is generally considered to be the gold standard. The authors noted and discussed some limitations of their analysis. Overall, the findings were clearly reported.

Concluding remarks:
Overall, the study was based on valid methodology and was well reported. The authors’ conclusions appear to be appropriate for the scope of their study.

Funding
Supported by grants from the Agency for Healthcare Research and Quality, and the American Board of Obstetrics and Gynecology/American Association of Obstetricians and Gynecologists Foundation.

Bibliographic details
Havrilesky LJ, Sanders GD, Kulasingam S, Myers ER. Reducing ovarian cancer mortality through screening: is it possible, and can we afford it? Gynecologic Oncology 2008; 111(2): 179-187

PubMedID
18722004

DOI
10.1016/j.ygyno.2008.07.006

Original Paper URL
http://dx.doi.org/10.1016/j.ygyno.2008.07.006

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Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Aged, 80 and over; Computer Simulation; Cost-Benefit Analysis; Female; Humans; Markov Chains; Mass Screening /economics /methods; Middle Aged; Models, Statistical; Neoplasm Staging; Ovarian Neoplasms /economics /mortality /pathology /prevention & control; Predictive Value of Tests; SEER Program; United States /epidemiology; Young Adult
AccessionNumber
22009100148

Date bibliographic record published
31/03/2009

Date abstract record published
09/12/2009