Screening for ovarian cancer: a systematic review
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Authors' objectives
The objectives of the authors were four-fold.

1. To evaluate the performance of current screening tests for ovarian cancer.

2. To assess the adverse effects of screening, including morbidity associated with surgical intervention and psychological morbidity associated with false-positive diagnosis.

3. To report on the stage of development of newer methods of screening.

4. To investigate the potential cost-effectiveness of screening in different risk groups.

Searching
Performance of the screening tests: Current Contents, MEDLINE (from 1966 to May 1997), EMBASE (from 1982 to May 1997), CINAHL (from 1982 to 1997), the Cochrane Controlled Trials Register (Issue 3, 1996) and Cancerlit (from 1966 to May 1997) were searched. Additional published and unpublished studies were identified by contacting researchers, experts in the field and consultants to the review, and by examining the bibliographies of relevant literature reviews. Conference proceedings were identified through Cancerlit.

Adverse effects of screening: MEDLINE (from 1982 to 1997), EMBASE (from 1982 to 1997), CINAHL and PsycLIT (from 1974 to 1997) were searched.

Cost-effectiveness of screening for ovarian cancer: EconLit, MEDLINE and NHS EED were searched for economic evaluation studies. In addition, studies reporting cost information were identified from the main search.

The search strategies were reported in full in the appendices to the report.

Study selection
Study designs of evaluations included in the review
Performance of the screening tests: only prospective screening studies (including randomised controlled trials, RCTs) were eligible for inclusion.

Adverse effects of screening: for studies assessing the psychological effects of screening, all study designs were eligible for inclusion. For assessing the adverse effects of surgery, only studies with more than 50 patients were eligible.

Cost-effectiveness of screening for ovarian cancer: any study reporting cost data for ovarian cancer screening was also eligible for inclusion.

Specific interventions included in the review
Studies evaluating any test or combination of tests to detect ovarian cancer were eligible for inclusion. The screening tests used in the included studies were ultrasound scanning, the measurement of the tumour marker cancer antigen 125 (CA-125) in serum, and colour Doppler imaging.

Reference standard test against which the new test was compared
The included studies were required to follow-up women testing positive with diagnostic surgery. In the review, the follow-up at one year was used to determine the sensitivity of the screening tests.

Participants included in the review
Performance of the screening tests: only studies of women with no clinical symptoms of ovarian cancer were eligible for inclusion. Studies of women already scheduled for surgical investigation were excluded.

Adverse effects of screening: for the assessment of psychological effects of screening, studies in the general population or in women at high risk were eligible for inclusion.

Outcomes assessed in the review
Performance of the screening tests: no inclusion criteria relating to outcome measures were specified. The outcome measures in the review were the calculated sensitivity, specificity, positive predictive value (PPV) and false-positive rates.

Adverse effects of screening: studies were eligible for inclusion if they reported on the surgical complications of procedures used in diagnosing ovarian cancer (such as open or laparoscopic oophorectomy), or on the psychological outcomes of screening. For studies on the adverse effects of surgery, studies of simultaneous oophorectomy and hysterectomy and studies of the long-term effects of oophorectomy were excluded.

How were decisions on the relevance of primary studies made?
For studies evaluating the performance of screening tests, three reviewers independently assessed the retrieved abstracts and titles for relevance; the full versions of selected papers were independently assessed for inclusion by two reviewers.

Assessment of study quality
Methodological quality was assessed based on criteria recommended by the Cochrane Methods Working Group on Systematic Reviews of Screening and Diagnostic Tests (see Other Publications of Related Interest no.1). Information relating to the following methodological issues was recorded: the method and completeness of follow-up of women with a negative screening outcome; the clarity of cut-off points and explicitness of the description of the protocol; the completeness of result reporting, including the drop-out rates at each stage of screening; and the description of the study population with respect to major risk factors. These factors were considered separately in assessing the validity of each study in relation to the different outcomes investigated.

The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The data were extracted by one reviewer using a standard data extraction form, and checked by a second reviewer.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative description.

How were differences between studies investigated?
Differences between the studies were discussed in the text.

Results of the review
Performance of the screening tests: 25 prospective screening studies were included, of which 16 screened women who were at average risk for their age of developing ovarian cancer (i.e. the results may be relevant to the general population). The size of the studies varied between 435 and 22,000 for these general population samples.

Adverse effects of screening: there were 3 studies reporting on the psychological effects of screening and 9 studies reporting on the complications of surgical investigation.

No completed RCTs of screening for ovarian cancer were identified.
Screening test performance.

Approximately 50% (95% confidence interval, CI: 23, 77) and 75% (95% CI: 35, 97) of the patients were diagnosed at Stage I in CA-125-based and ultrasound screening studies, respectively. Annual screening with ultrasound appeared to have a sensitivity or detection rate close to 100%. The reported sensitivity of annual CA-125-based screening was approximately 80%. The false-positive result rate was around 1.2 to 2.5% for women screened by ultrasound scanning, and 0.1 to 0.6% for CA-125-based screening. Approximately 0.5 to 1% of women will suffer a significant complication due to surgery, and most of those who do not have ovarian cancer will have a benign gynaecological condition. The proportion of screened women who are recalled for further testing and assessment, resulting in potential distress and anxiety to otherwise healthy women, is around 3 to 12%.

The impact of screening for ovarian cancer.

The PPVs of ovarian screening were low: 3% for surgery and 0.6% for initial recall for annual ultrasound screening; 15% for surgery and 1% for initial recall for annual CA-125-based screening. This is due mainly to the relatively low prevalence of ovarian cancer. The evidence suggests that ultrasound screening is more sensitive than CA-125-based screening, although the latter may result in fewer false-positives and, hence, a higher PPV. It was suggested that the addition of colour Doppler imaging to ultrasound screening may reduce the false-positive rate; however, variable results have been reported.

Screening a higher-risk population: there was a lack of evidence on whether screening women at higher risk could reduce the mortality of ovarian cancer.

Cost information

It was suggested that the cost of screening a woman with ultrasound is higher than the cost for CA-125 testing followed by ultrasound screening.

Authors’ conclusions

The relatively low prevalence of ovarian cancer means that the PPV of screening tests is low. Since surgery is the consequence of a false-positive result, it is important to consider the overall impact of screening for ovarian cancer. The low prevalence also limits the potential cost-effectiveness of population screening. Screening women who are at risk because of a strong family history may be more cost-effective, but this has not been established. Further evidence is required before a decision can be made concerning the potential benefits, harms and costs of screening for ovarian cancer.

CRD commentary

This review was conducted according to structured guidelines for systematic reviews. The literature search was comprehensive, the inclusion criteria were clearly described, and the validity of the included studies was assessed. Details of the included and excluded studies were clearly reported. The narrative summary used was appropriate given the extent of heterogeneity in the screening tests and cut-off values used, and the populations studied. Deficiencies in the existing evidence-base were extensively discussed, and the authors’ conclusions were suitably cautious.

Implications of the review for practice and research

Practice: The authors do not make any specific recommendations for practice.

Research: The authors state the following.

1. Assessment of the adverse effects of screening and the relative cost-effectiveness of different screening strategies would enhance information from RCTs of screening that are currently in progress.

2. New or modified screening tests should be compared with those being evaluated in current trials. Test developments requiring further evaluation include: the impact of adding CDI to ultrasound screening; the use of CA-125 levels in
multivariate algorithms to determine thresholds for ultrasound and surgical intervention; and the marginal value of adding CA-125 to ultrasound screening. Screening modalities will require continuous re-evaluation in line with technical developments.

3. Research should be directed towards evaluating both the clinical and cost-effectiveness of screening strategies for patients at high risk.

4. Research into the impact of genetic testing on health outcomes, and the level of demand for such services, is also needed.

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