Supplementary Online Content


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This supplementary material has been provided by the authors to give readers additional information about their work.
eMethods. Literature Search Strategies for Primary Literature

Key:
/ = MeSH subject heading
$ = truncation
* = truncation
? = wildcard
ab = word in abstract
adj# = adjacent within x number of words
ae = adverse effects
hw = subject heading word
id = identifier
kw = keyword
md = methodology
near/# = adjacent within x number of words
ti = word in title

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 (ovar* or (fallopian next tub*) or adenx*):ti,ab,kw near/4 (cancer* or neoplas* or tumo* or malignan* or carcinoma* or adenocarcinoma* or mass*):ti,ab,kw
#2 screen*:ti,ab,kw
#3 detect*:ti
#4 (sonog* or ultraso*):ti,ab,kw
#5 (tumo* next marker*):ti,ab,kw
#6 (serum next cancer next antigen*):ti,ab,kw
#7 "CA 125":ti,ab,kw
#8 #1-#7
#9 #1 and #8 Publication Year from 2003 to 2016, in Trials

MEDLINE
1 Ovarian Neoplasms/
2 Fallopian Tube Neoplasms/
3 ((ovar$ or fallopian tub$ or adenx$) adj4 (cancer$ or neoplas$ or tumo$ or malignan$ or carcinoma$ or adenocarcinoma$ or mass$)).ti,ab.
4 or/1-3
5 Mass screening/
6 "Early detection of cancer"/
7 (screen$ adj5 (ovar$ or fallopian tub$ or adnex$)).ti,ab.
8 detect$.ti.
9 Ultrasonography/
10 (sonog$ or ultraso$).ti,ab.
11 Tumor Markers, Biological/
12 tumo?r marker$.ti,ab.
13 serum cancer antigen$.ti,ab.
14 CA 125.ti,ab.
15 algorithm$.ti,ab.
16 ROCA.ti,ab.
17 or/5-16
18 4 and 17
19 Ovarian Neoplasms/us [Ultrasonography]
20 Fallopian Tube Neoplasms/us [Ultrasonography]
21 18 or 19 or 20
22 clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled

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trials as topic/ or meta-analysis as topic/
23 (clinical trial or controlled clinical trial or meta analysis or randomized controlled trial).pt.

24 Random$.ti,ab.
25 control groups/ or double-blind method/ or single-blind method/
26 clinical trial$.ti,ab.
27 controlled trial$.ti,ab.
28 meta analy$.ti,ab.
29 or/22-28
30 21 and 29
31 Animals/ not (Humans/ and Animals/)
32 30 not 31
33 limit 32 to (english language and yr="2003 -Current")
34 remove duplicates from 33

PUBMED, publisher-supplied records
#14 Search (((#13) AND publisher[sb]) AND ("2003/01/01"[Date - Publication] : "3000"[Date - Publication])) AND English[Language]
#13 Search #8 AND #12
#12 Search #9 OR #10 OR #11
#11 Search (control[tiab] OR controls[tiab] OR controlled[tiab] OR controled[tiab]) AND (trial[tiab] OR trials[tiab])
#10 Search "clinical trial"[tiab] OR "clinical trials"[tiab] OR random*[tiab]
#9 Search systematic review[sb] OR metaanaly*[tiab] OR meta analysis[tiab]
#8 Search #1 AND #7
#7 Search #2 OR #3 OR #4 OR #5 OR #6
#6 Search CA 125[tiab]
#5 Search serum cancer antigen*[tiab]
#4 Search tumo* marker*[tiab]
#3 Search sonog*[tiab] or ultraso*[tiab]
#2 Search screen*[tiab] OR detect*[tiab]
#1 Search (ovar*[tiab] or fallopian tub*[tiab] or adenx*[tiab]) AND (cancer*[tiab] or neoplas*[tiab] or tumor*[tiab] OR tumour*[tiab] or malignan*[tiab] or carcinoma*[tiab] or adenocarcinoma*[tiab] or mass*[tiab])
## eTable 1. Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Category</th>
<th>Included</th>
<th>Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aim</td>
<td>Screening for ovarian cancer in a primary care setting (alone or as part of a clinical examination)</td>
<td>Screening for ovarian cancer in selected high-risk populations, such as women who are BRCA mutation carriers or patients of a specialty practice, such as oncology</td>
</tr>
<tr>
<td>Populations</td>
<td>Asymptomatic, average risk women, ages 45 years and older</td>
<td>Trials enrolling only women who are selected based on an increased risk for ovarian cancer (e.g. known predisposing genetic syndromes, strong family history)</td>
</tr>
<tr>
<td>Screening tests</td>
<td>Screening tests and approaches evaluated in clinical trials such as, but not limited to: testing for serum cancer antigen (CA–125), transvaginal ultrasonography, and combined screening approaches or algorithms</td>
<td>Screening tests not evaluated in clinical trials</td>
</tr>
<tr>
<td>Comparisons</td>
<td>Comparison of screening with usual care or no screening; comparison of different included screening methods or programs</td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td><strong>KQ 1</strong>: Ovarian cancer–specific mortality (including primary peritoneal and fallopian tube cancer), all-cause mortality, cancer-related morbidity, and quality of life. <strong>KQ 2</strong>: Surgery rate, rates of false-positive screening results, complications of diagnostic surgical procedures, and health and psychological effects of screening tests</td>
<td></td>
</tr>
<tr>
<td>Settings</td>
<td>Primary care settings, including obstetrics/gynecology practices</td>
<td>Specialty practice settings, such as oncology</td>
</tr>
<tr>
<td>Study designs</td>
<td>Randomized, controlled trials</td>
<td>Cohort studies, case-controls, case reports, case series, and decision analyses</td>
</tr>
<tr>
<td>Study quality</td>
<td>Good and fair quality according to USPSTF criteria and supplemented quality measures</td>
<td>Poor quality according to USPSTF criteria and supplemental quality measures</td>
</tr>
<tr>
<td>Language</td>
<td>English</td>
<td>Non–English language studies</td>
</tr>
</tbody>
</table>

**Abbreviations**: USPSTF, United States Preventive Services Task Force
# eTable 2. Quality Assessment Criteria of Randomized Controlled Trials

<table>
<thead>
<tr>
<th>USPSTF quality rating criteria¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Initial assembly of comparable groups employs adequate randomization, including first concealment and whether potential confounders were distributed equally among groups</td>
</tr>
<tr>
<td>- Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination)</td>
</tr>
<tr>
<td>- Important differential loss to followup or overall high loss to followup</td>
</tr>
<tr>
<td>- Measurements: equal, reliable, and valid (includes masking of outcome assessment)</td>
</tr>
<tr>
<td>- Clear definition of the interventions</td>
</tr>
<tr>
<td>- All important outcomes considered</td>
</tr>
<tr>
<td>- Intention-to-treat analysis</td>
</tr>
</tbody>
</table>

¹ Good quality studies generally meet all quality criteria. Fair quality studies do not meet all the criteria but not have critical limitations that could invalidate study findings. Poor quality studies have a single fatal flaw or multiple important limitations that could invalidate study findings. Critical appraisal of studies using a priori quality criteria are conducted independently by at least two reviewers. Disagreements in final quality assessment are resolved by consensus, and, if needed, consultation with a third independent reviewer.

Abbreviations: USPSTF, U.S. Preventive Services Task Force
### Table 3. Harms Reported in Ovarian Cancer Screening Trials: Psychological Effects of Screening

<table>
<thead>
<tr>
<th>Trial, Author, Year of publication</th>
<th>UKCTOCS (Barrett, 2014)*</th>
<th>QUEST, 2007*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality</td>
<td>Good</td>
<td>Fair</td>
</tr>
</tbody>
</table>
| Measures                           | Spielberger State/Trait Anxiety Inventory  
General Health Questionnaire 12 | SF-36 Mental and Physical Health scores (quality of life)  
Impact of Events Scale (distress)  
Modified Lerman cancer worry scale (cancer worry) |
| Population                        | Random sample from UKCTOCS | Event sample: All women in the screening arms recalled for repeat screening* |
|                                   |                          | All participants |
| N analyzed                        | CA-125 ROCA: 301  
TVU: 283  
Control: 755 | CA-125 ROCA: 12,357  
TVU: 9,678 | Screening group: 292  
Control: 150 |
| Psychological effect of screening | Random sample: no evidence of difference in state anxiety between screening and control groups (P= 0.2) | NA |
|                                   |                          | No statistically significant differences between study arms in measures of quality of life, distress, or cancer worry (P = NR) |
| Psychological effects of positive test results or repeat screening tests | No evidence of change in anxiety (P= 0.36) or psychological morbidity (P= 0.96) due to repeat screenings compared with annual screen | Evidence of higher anxiety for multiple repeat scans (p<0.010) (small absolute effect)* compared with a single repeat screen |
|                                   |                          | Greater odds of psychological morbidity (GHQ-12: score ≥ 4) with higher level referral screening: OR 1.28 (95% CI, 1.18 to 1.39)* |
|                                   |                          | Women with abnormal test results (N= 32) compared with women with no abnormal results more likely to report increased levels of cancer worry at 2-year followup: OR 2.8 (95% CI, 1.1 to 7.2) |

*Excluding those in the random sample analysis  
* Difference in Spielberger State/Trait Anxiety Inventory score (range 20-80 points): 0.37 (95% CI 0.23 0.51; P < 0.01)  
* Higher level referral- CA-125 ROCA: repeat blood test and a transvaginal scan, TVU: repeat scan or biopsy

**Abbreviations:** CG = control group; CI = confidence interval; GHQ-12 = General Health Questionnaire 12; NR = not reported; OR = odds ratio; QoL = quality of life; QUEST = Quality of life, Education, and Screening Trial; ROCA = Risk of Ovarian Cancer Algorithm TVU = transvaginal ultrasound; SF-36 = 36-Item Short Form Survey; UKCTOCS = U.K. Collaborative Trial of Ovarian Cancer Screening

### eReferences

