Screening for Ovarian Cancer: U.S. Preventive Services Task Force Reaffirmation Recommendation Statement

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Description: Reaffirmation of the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for ovarian cancer.

Methods: A 2008 review of the literature commissioned by the USPSTF revealed no new evidence about the benefits of screening for ovarian cancer but provided some new data about observed harms of screening. A bridge search to 2011 focused on evidence from randomized, controlled trials.

Population: This recommendation applies to asymptomatic women. It does not apply to women with known genetic mutations that increase their risk for ovarian cancer (for example, BRCA mutations).

Recommendation: The USPSTF recommends against screening for ovarian cancer in women (D recommendation).

Ann Intern Med. 2012;157:900-904. www.annals.org

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* For a list of USPSTF members, see the **Appendix** (available at www.annals.org).

This article was published at www.annals.org on 11 September 2012.

The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific clinical preventive services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

SUMMARY OF RECOMMENDATION AND EVIDENCE

The USPSTF recommends against screening for ovarian cancer in women (D recommendation).

This recommendation applies to asymptomatic women. Women with known genetic mutations that increase their risk for ovarian cancer (for example, BRCA mutations) are not included in this recommendation.

See also:

Print
Summary for Patients I-56

Web-Only
CME quiz (preview on page I-34)
Consumer Fact Sheet

See the **Figure** for a summary of the recommendation and suggestions for clinical practice and **Appendix Tables 1** and **2** (available at www.annals.org) for the USPSTF grades and classification of levels of certainty about net benefit.

RATIONALE

Importance

Ovarian cancer has the highest mortality rate of all types of gynecologic cancer and is the fifth-leading cause of cancer death among women.

Detection

Although the mortality rate associated with ovarian cancer is high, the disease occurs infrequently in the general U.S. population, with an age-adjusted incidence of 13 cases per 100 000 women. As a result, the positive predictive value of screening for ovarian cancer—which directly depends on the prevalence of the disease—is low, and most women with a positive screening test result will have a false-positive result.

Benefits of Detection and Early Intervention and Treatment

The USPSTF found adequate evidence that annual screening with transvaginal ultrasonography and testing for a serum tumor marker, cancer antigen (CA)–125, in women does not reduce the number of ovarian cancer deaths.

Harms of Detection and Early Intervention and Treatment

Adequate evidence shows that screening for ovarian cancer can lead to important harms, including major surgical interventions in women who do not have cancer.

Figure. **Screening for ovarian cancer: clinical summary of U.S. Preventive Services Task Force recommendation.**

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SCREENING FOR OVARIAN CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Asymptomatic women without known genetic mutations that increase risk for ovarian cancer
Recommendation	**Do not screen for ovarian cancer.**
	Grade: D

Risk Assessment	Women with *BRCA1* and *BRCA2* genetic mutations, the Lynch syndrome (hereditary nonpolyposis colon cancer), or a family history of ovarian cancer are at increased risk for ovarian cancer. Women with an increased-risk family history should be considered for genetic counseling to further evaluate their potential risks. "Increased-risk family history" generally means having 2 or more first- or second-degree relatives with a history of ovarian cancer or a combination of breast and ovarian cancer; for women of Ashkenazi Jewish descent, it means having a first-degree relative (or 2 second-degree relatives on the same side of the family) with breast or ovarian cancer.
Screening Tests	Transvaginal ultrasonography and serum cancer antigen (CA)–125 testing are the most commonly suggested screening tests.
Treatments	Treatment of ovarian carcinoma includes surgical treatment (debulking) and intraperitoneal or systemic chemotherapy.
Balance of Benefits and Harms	Annual screening with transvaginal ultrasonography and serum CA-125 testing in women does not decrease ovarian cancer mortality. Screening for ovarian cancer can lead to important harms, including major surgical interventions in women who do not have cancer. Therefore, the harms of screening for ovarian cancer outweigh the benefits.
Other Relevant USPSTF Recommendations	The USPSTF has made a recommendation on genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility. This recommendation is available at www.uspreventiveservicestaskforce.org.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

USPSTF Assessment

The USPSTF concludes that there is at least moderate certainty that the harms of screening for ovarian cancer outweigh the benefits.

Clinical Considerations

Patient Population

This recommendation applies to asymptomatic women. Women with known genetic mutations that increase their risk for ovarian cancer (for example, BRCA mutations) are not included in this recommendation.

Risk Assessment

Women with *BRCA1* and *BRCA2* genetic mutations, the Lynch syndrome (hereditary nonpolyposis colon cancer), or a family history of ovarian cancer are at increased risk for ovarian cancer. Although no standardized referral criteria currently exist, women with an increased-risk family history should be considered for genetic counseling to further evaluate their potential risks. "Increased-risk family history" generally means having 2 or more first- or second-degree relatives with a history of ovarian cancer or a combination of breast and ovarian cancer; for women of Ashkenazi Jewish descent, it means having a first-degree relative (or 2 second-degree relatives on the same side of the family) with breast or ovarian cancer.

Women with a family history of ovarian cancer were not excluded from most randomized screening trials. In the only trial reporting ovarian cancer mortality results, women with a family history of ovarian or breast cancer comprised 17% of the participants. The overall trial showed no mortality benefit; outcomes were not separately reported for this subgroup. Although available evidence does not show with absolute certainty whether the balance of benefits and harms of ovarian cancer screening may differ for women with a family history of ovarian cancer, the USPSTF found no reason to believe that such women would necessarily benefit. A higher incidence of cancer may result in more diagnoses and treatments, but the increase may not be accompanied by a reduction in deaths and may actually lead to more associated harms. An ongoing prospective cohort study, the United Kingdom Familial Ovarian Cancer Screening Study, may help to resolve some of these questions.

Factors associated with a reduced risk for ovarian cancer include the use of oral contraceptives, pregnancy and breastfeeding, bilateral tubal ligation, and removal of the ovaries.

Screening Tests

Transvaginal ultrasonography and serum CA-125 testing are readily available procedures and commonly suggested screening methods. The bimanual pelvic examination is often conducted (usually annually) in part to screen for ovarian cancer, although its effectiveness and harms are not well-known and were not a focus of this review.

The evaluation of abnormal test results consists of either repeated testing or, frequently, removal of one or both of the ovaries by means of laparoscopy or laparotomy.

Treatment

Treatment of ovarian carcinoma includes surgical treatment (debulking) and intraperitoneal or systemic chemotherapy.

Useful Resources

In its recommendation on genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility, the USPSTF recommends that women with a family history indicating that they are at risk for a deleterious mutation be referred for genetic counseling and testing. More information on this recommendation can be found at www.uspreventiveservicestaskforce.org.

Discussion

In 2004, the USPSTF reviewed the evidence for screening for ovarian cancer and found that the potential harms outweighed the potential benefits of screening (1). A 2008 review of the literature commissioned by the USPSTF revealed no new evidence about the benefits of screening for ovarian cancer but provided some new data about observed harms of screening (2). In 2011, the USPSTF commissioned a bridge search to update the 2008 review, focusing on evidence available from randomized, controlled trials (3).

A single randomized, controlled trial, the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial (4), has published mortality results associated with screening for ovarian cancer in asymptomatic, average-risk women using serum CA-125 testing (positive threshold of ≥35 kU/L [≥35 U/mL]) and transvaginal ultrasonography. In this trial, 78 216 women in the United States were randomly assigned to either annual screening (6 years for CA-125 testing and 4 years for transvaginal ultrasonography) or usual care and were followed for up to 13 years. Women were considered eligible if they were between 55 and 74 years of age and had no previous diagnosis of lung, colorectal, or ovarian cancer. Two initial exclusion criteria (previous oophorectomy and current tamoxifen use) were dropped during the recruitment phase. Nearly 90% of women were white, and 17% had a family history of breast or ovarian cancer. Management of abnormal test results was directed by the participant's personal health care provider. Although there was a nonstatistically significant finding of an increased number of ovarian cancer cases diagnosed in the screening group compared with the control group (212 vs. 176 cases; relative risk, 1.21 [95% CI, 0.99 to 1.48]), no difference was found in either stage at diagnosis or ovarian cancer death rate (118 vs. 100 deaths; relative risk, 1.18 [CI, 0.82 to 1.71]) (4). The low degree of contamination (<5%) and high rate of screening adherence (approximately 80%) seen during the trial, coupled with the lack of difference in stage at diagnosis, bolster the trial's finding that screening average-risk, asymptomatic women with serum CA-125 testing and transvaginal ultrasonography does not reduce ovarian cancer deaths.

Harms associated with screening for ovarian cancer have been reported by several trials. In the PLCO Cancer Screening Trial, approximately 10% of participants in the screening group received a false-positive result during the trial; the positive predictive value of CA-125 testing and transvaginal ultrasonography screening was just greater than 1% across all screening rounds (5). One third of women with a false-positive result had an oophorectomy, with an overall ratio of surgeries to screen-detected ovarian cancer of approximately 20:1. Nearly 21 major complications occurred per 100 surgical procedures done on the basis of false-positive screening results (4). A randomized trial set within the Shizuoka Cohort Study of Ovarian Cancer Screening evaluated the use of transvaginal or transabdominal ultrasonography in conjunction with serum CA-125 testing (positive threshold of >35 kU/L [>35 U/mL]) and reported that an estimated 33 surgeries were required to diagnose 1 case of screen-detected ovarian cancer (6).

An ongoing randomized trial, UKCTOCS (United Kingdom Collaborative Trial of Ovarian Cancer Screening), is evaluating the effect of annual screening with serum CA-125 testing and transvaginal ultrasonography follow-up for abnormal results, as determined by an ovarian cancer risk algorithm, taking into account age, absolute CA-125 level, and CA-125 trajectory over time, compared with annual screening with transvaginal ultrasonography or no screening. Data are available only from the pilot trial and the baseline (prevalence) screening round of the full trial. In the pilot, nearly 20% of women in the multimethod group who participated in the first screening were initially categorized as being at intermediate risk for ovarian cancer and required up to 5 additional blood tests before being returned to the low-risk pool. Less than 1% of participants had surgery to investigate an abnormal screening result (compared with approximately 2% in the PLCO Cancer Screening Trial); however, of the 16 women who had surgery, 11 (69%) did not have ovarian cancer (7). In the full trial, approximately 9% of women receiving baseline multimethod screening required repeated testing for abnormal results and less than 1% of women had surgery.

Among women having surgery for a false-positive result (47 of 97 women [48%]), approximately 4% had a major complication (8).

No randomized trial has assessed the role of the bimanual pelvic examination for cancer screening. In the PLCO Cancer Screening Trial, bimanual examination was discontinued as a screening strategy in the intervention group because no cases of ovarian cancer were detected solely by this method and a high proportion of women had bimanual examination with ovarian palpation in the usual care group.

The USPSTF concludes that there is adequate evidence that there is no mortality benefit to routine screening for ovarian cancer with transvaginal ultrasonography or single-threshold serum CA-125 testing and that the harms of such screening are at least moderate. Final results from UKCTOCS should provide more information about the relative benefits and harms of an algorithm-based approach to screening for ovarian cancer.

Response to Public Comments

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 10 April to 8 May 2012. In response to comments, the USPSTF clarified language describing what is meant by increased risk for ovarian cancer, what is known about ovarian cancer screening in women with a family history of the disease, and the diagnostic pathway for abnormal screening results.

Several commenters asked the USPSTF to provide information about other potential screening methods—in particular, a large panel biomarker screening test, OvaDx (Arrayit Corporation, Sunnyvale, California). The OvaDx test is not currently approved by the U.S. Food and Drug Administration for clinical use in ovarian cancer screening (it was submitted to the U.S. Food and Drug Administration for review in August 2010); pilot studies of its test characteristics are in progress (9). In the systematic evidence review commissioned by the USPSTF, which focused on randomized, controlled trials of screening with ovarian cancer morbidity or mortality as the outcomes of interest, no trials with these clinical outcomes were identified for any testing methods besides serum CA-125 testing and transvaginal ultrasonography, meaning that there is currently limited evidence to assess the ultimate health effects of other potential screening tests for ovarian cancer.

Commenters asked the USPSTF to include specific guidance or information about the potential role of symptoms in the earlier detection of ovarian cancer. The primary mission of the USPSTF is to make recommendations on clinical preventive services for average-risk persons without signs or symptoms of disease. As such, a search for data on the use of symptoms to guide detection of ovarian cancer was outside the scope of the commissioned systematic evidence review used to inform this recommendation statement. However, a literature search reveals that there is limited evidence available about the ultimate effectiveness of a combined symptoms-based approach with ancillary CA-125 testing or transvaginal ultrasonography; ovarian cancer morbidity and mortality were not specified or reported in available studies (10, 11). Symptoms included in the available studies were nonspecific in nature, including various gastrointestinal, urinary, gynecologic, and constitutional symptoms. Of note, 95% of women presenting to a primary care clinic report having at least 1 of these symptoms within the previous year, suggesting that there may be important inherent challenges related to the reliability of incorporating these nonspecific symptoms into ovarian cancer screening and diagnostic testing decisions (12).

Recommendations of Other Groups

Consensus among major medical and public health organizations is that screening for ovarian cancer in the general population is not recommended. The American Congress of Obstetricians and Gynecologists does not recommend screening for ovarian cancer in asymptomatic women; evaluation of high-risk persons may include transvaginal ultrasonography and CA-125 testing in addition to physical examination (13). The American Cancer Society states that no screening test has proven to be effective and sufficiently accurate for early detection of ovarian cancer. However, for women who are at high risk, the combination of a thorough pelvic examination, transvaginal ultrasonography, and a blood test for the tumor marker CA-125 may be offered (14).

From the U.S. Preventive Services Task Force, Rockville, Maryland.

Financial Support: The USPSTF is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.

Potential Conflicts of Interest: Disclosure forms from USPSTF members can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-2035.

Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.uspreventiveservicestaskforce.org).

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In the Clinic

In the Clinic is a monthly feature in *Annals* that focuses on practical management of patients with common clinical conditions. It offers evidence-based answers to frequently asked questions about screening, prevention, diagnosis, therapy, and patient education and provides physicians with tools to improve the quality of care. In the Clinic includes links to PIER and continiuing medical education quizzes offering category 1 CME credit.

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Appendix: U.S. Preventive Services Task Force

Members of the U.S. Preventive Services Task Force† at the time this recommendation was finalized are Virginia A. Moyer, MD, MPH, *Chair* (Baylor College of Medicine, Houston, Texas); Michael L. LeFevre, MD, MSPH, *Co-Vice Chair* (University of Missouri School of Medicine, Columbia, Missouri); Albert L. Siu, MD, MSPH, *Co-Vice Chair* (Mount Sinai School of Medicine, New York, and James J. Peters Veterans Affairs Medical Center, Bronx, New York); Linda Ciofu Baumann, PhD, RN (University of Wisconsin, Madison, Wisconsin); Kirsten Bibbins-Domingo, PhD, MD (University of California, San Francisco, San Francisco, California); Susan J. Curry, PhD (University of Iowa College of Public Health, Iowa City, Iowa); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Glenn Flores, MD (University of Texas Southwestern, Dallas, Texas); Adelita Gonzales Cantu, RN, PhD (University of Texas Health Science Center, San Antonio, Texas); David C. Grossman, MD, MPH (Group Health Cooperative, Seattle, Washington); Jessica Herzstein, MD, MPH (Air Products, Allentown, Pennsylvania); Joy Melnikow, MD, MPH (University of California, Davis, Sacramento, California); Wanda K. Nicholson, MD, MPH, MBA (University of North Carolina School of Medicine, Chapel Hill, North Carolina); Douglas K. Owens, MD, MS (Veteran Affairs Palo Alto Health Care System, Palo Alto, and Stanford University, Stanford, California); Carolina Reyes, MD, MPH (Virginia Hospital Center, Arlington, Virginia); and Timothy J. Wilt, MD, MPH (University of Minnesota Department of Medicine and Minneapolis Veteran Affairs Medical Center, Minneapolis, Minnesota).

† For a list of current USPSTF members, go to www.uspreventiveservicestaskforce.org/members.htm.

Appendix Table 1. What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	*Note: The following statement is undergoing revision.* Clinicians may provide this service to selected patients depending on individual circumstances. However, for most individuals without signs or symptoms, there is likely to be only a small benefit from this service.	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Appendix Table 2. USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; limited generalizability of findings to routine primary care practice; and lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies; important flaws in study design or methods; inconsistency of findings across individual studies; gaps in the chain of evidence; findings that are not generalizable to routine primary care practice; and a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

* The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.