American College of Radiology
ACR Appropriateness Criteria®
Ovarian Cancer Screening

Variant: 1 Adult. Ovarian cancer screening. Postmenopausal. Average risk.

Procedure	Appropriateness Category	Relative Radiation Level
US color Doppler ovaries	Usually Not Appropriate	O
US pelvis transabdominal	Usually Not Appropriate	O
US pelvis transvaginal	Usually Not Appropriate	O
MRI pelvis without and with IV contrast	Usually Not Appropriate	O
MRI pelvis without IV contrast	Usually Not Appropriate	O
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

Variant: 2 Adult. Ovarian cancer screening. Premenopausal. Average risk.

Procedure	Appropriateness Category	Relative Radiation Level
US color Doppler ovaries	Usually Not Appropriate	O
US pelvis transabdominal	Usually Not Appropriate	O
US pelvis transvaginal	Usually Not Appropriate	O
MRI pelvis without and with IV contrast	Usually Not Appropriate	O
MRI pelvis without IV contrast	Usually Not Appropriate	O
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

Variant: 3 Adult. Ovarian cancer screening. Premenopausal. High risk.

Procedure	Appropriateness Category	Relative Radiation Level
US color Doppler ovaries	May Be Appropriate	O
US pelvis transabdominal	May Be Appropriate	O
US pelvis transvaginal	May Be Appropriate	O
MRI pelvis without and with IV contrast	Usually Not Appropriate	O
MRI pelvis without IV contrast	Usually Not Appropriate	O
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

Variant: 4 Adult. Ovarian cancer screening. Postmenopausal. High risk.

Procedure	Appropriateness Category	Relative Radiation Level
US color Doppler ovaries	May Be Appropriate	O

US pelvis transabdominal	May Be Appropriate	O
US pelvis transvaginal	May Be Appropriate	O
MRI pelvis without and with IV contrast	Usually Not Appropriate	O
MRI pelvis without IV contrast	Usually Not Appropriate	O
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

Panel Members

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Summary of Literature Review

Introduction/Background

Ovarian cancer remains low in prevalence, with a lifetime risk of approximately 1.1% in the general population, but has the highest mortality of all gynecologic malignancies. In 2024, there will be an estimated 19,680 new cases of ovarian cancer and 12,740 deaths [1]. Ovarian cancer can affect anyone who has ovaries, including cisgender women as well as transgender men and nonbinary people who have ovaries. Risk factors that increase the likelihood for the development of ovarian cancer include the presence of *BRCA1* or *BRCA2* mutations, strong family history (ie, first-degree relative, particularly if premenopausal at the time of diagnosis), nulliparity, lack of breastfeeding, lack of hormonal contraception use, and postmenopausal status [2]. Among all risk factors, a genetic predisposition is associated with the highest increase in cancer risk, with mutations in the *BRCA1/2* genes increasing the risk of ovarian cancer to 39% by age 70 years for *BRCA1* mutations and 10% to 17% by age 70 years for *BRCA2* mutations [3-5]. Ovarian cancers comprise a heterogeneous group of malignancies arising from or involving the ovary, subdivided into epithelial ovarian cancers, the most common type (90% of cases), and nonepithelial cancers (10% of cases) [6]. Epithelial ovarian cancers are further subdivided into type I and type II subtypes based upon their clinical behavior and pathologic features, with each subtype having distinct risk factors and putative precursor lesions. Type II ovarian cancers, typified by mutations in the *TP53* tumor suppressor gene, are the most common and most aggressive of the ovarian cancers and are also associated with *BRCA1* and *BRCA2* mutations. Their corresponding histologies include high-grade serous (the most common subtype, usually advanced stage at presentation), high-grade endometrioid, carcinosarcoma, and undifferentiated carcinomas [6]. Type I tumors are less aggressive than Type II and include low-grade serous, low-grade endometrioid, clear cell carcinomas, and mucinous carcinomas [6].

Population-based screening for ovarian cancer remains a topic of ongoing interest in contemporary practice, given that the majority of ovarian cancers encountered are high-grade aggressive malignancies, for which favorable survival rates are encountered in the setting of early-

stage disease. If ovarian cancer is detected early, the 5-year survival rates are 90% if confined to the ovary (stage I) or 70% if confined to the pelvis (stage II) [6]. However, most ovarian cancers are diagnosed at stages III (51%) and IV (29%) in which where 5-year survival rates are less than 30% [7,8]. Overall, 5-year survival ranges between 30% and 40% worldwide and has increased little (2%-4%) over the last 2 decades [9,10]. Additionally, 70% of patients with advanced epithelial ovarian cancer will have cancer recurrence, after which time survival is extremely low [6]. Although this current literature review demonstrates no evidence to support screening patients of average-risk (ie, those with no personal or family history of breast or ovarian cancer, no known or suspected genetic predisposition, or elevated serum cancer antigen 125 [CA 125] level), the evidence summarized in this update may lend support to future prospective studies combining the use of imaging with serum biomarkers in select cases.

Discussion of Procedures by Variant

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.

The goal of ovarian cancer screening is early detection of ovarian cancer before it being detected clinically and before the onset of locally advanced or metastatic disease. Appropriate and effective imaging for ovarian cancer screening can confirm the presence of ovarian cancer at an earlier stage than via clinical assessment, thereby guiding management. The expected outcome for effective ovarian cancer screening is decreased burden of disease.

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
A. CT abdomen and pelvis with IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis with intravenous (IV) contrast for ovarian cancer screening in postmenopausal patients without risk factors. Although CT is routinely used for ovarian cancer staging, its limited ability to evaluate the adnexa and accurately distinguish between benign and malignant ovarian lesions makes it an impractical screening tool in this setting. In a prior study of 2,869 postmenopausal patients undergoing CT screening colonography, in whom 118 (4.1%) were found to have incidentally detected adnexal lesions, no ovarian cancers were identified in those patients who underwent further workup with surgical resection. Moreover, 4 patients in the study cohort who subsequently developed ovarian cancer were noted to have had a prior negative CT examination [11].

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
B. CT abdomen and pelvis without and with IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis without and with IV contrast for ovarian cancer screening in postmenopausal patients without risk factors. Although CT is routinely used for ovarian cancer staging, its limited ability to evaluate the adnexa and accurately distinguish between benign and malignant ovarian lesions makes it an impractical screening tool in this setting. In a prior study of 2,869 postmenopausal patients undergoing CT screening colonography, in whom 118 (4.1%) were found to have incidentally detected adnexal lesions, no ovarian cancers were identified in those patients who underwent further workup with surgical resection. Moreover, 4 patients in the study cohort who subsequently developed ovarian cancer were noted to have had a prior negative CT examination [11].

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
C. CT abdomen and pelvis without IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis without IV

contrast for ovarian cancer screening in postmenopausal patients without risk factors. Although CT is routinely used for ovarian cancer staging, its limited ability to evaluate the adnexa and accurately distinguish between benign and malignant ovarian lesions makes it an impractical screening tool in this setting. In a prior study of 2,869 postmenopausal patients undergoing CT screening colonography, in whom 118 (4.1%) were found to have incidentally detected adnexal lesions, no ovarian cancers were identified in those patients who underwent further workup with surgical resection. Moreover, 4 patients in the study cohort who subsequently developed ovarian cancer were noted to have had a prior negative CT examination [11].

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
D. FDG-PET/CT skull base to mid-thigh

Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT is a useful imaging modality for the staging of cancer and detection of cancer recurrence. However, there is no relevant literature to support the use of FDG-PET/CT from the skull base to mid-thigh for ovarian cancer screening in postmenopausal patients without risk factors.

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
E. MRI pelvis without and with IV contrast

There is no relevant literature to support the use of MRI of the pelvis without and with IV contrast for ovarian cancer screening in postmenopausal patients without risk factors. MRI is a useful imaging modality for the characterization of indeterminate mass detected on ultrasound (US) [10]. However, it has not been used for population-based screening given its unconfirmed benefit in this setting.

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
F. MRI pelvis without IV contrast

There is no relevant literature to support the use of MRI of the pelvis without IV contrast for ovarian cancer screening in postmenopausal patients without risk factors. MRI is a useful imaging modality for the characterization of indeterminate mass detected on US [10]. However, it has not been used for population-based screening given its unconfirmed benefit in this setting.

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
G. US color Doppler ovaries

There is no relevant literature to support the use of color Doppler US assessment of the ovaries for ovarian cancer screening in postmenopausal patients without risk factors. Most studies discussed in this document have addressed the use of transvaginal US for ovarian cancer screening in average-risk postmenopausal patients. Even though color Doppler is performed as part of routine transvaginal US studies, the published literature to date has lacked the methodologic detail to confirm any benefit from Doppler assessment in these patients. No explicit benefit from color Doppler has been reported in postmenopausal patients without risk factors [12-19].

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
H. US pelvis transabdominal

There is no relevant literature to support the use of transabdominal pelvic US for ovarian cancer screening in postmenopausal patients without risk factors. Most studies discussed in this document have addressed the use of transvaginal US for ovarian cancer screening in average-risk postmenopausal patients [12-19].

Variant 1: Adult. Ovarian cancer screening. Postmenopausal. Average risk.
I. US pelvis transvaginal

Transvaginal US of the pelvis is the imaging modality that has been most commonly evaluated for ovarian cancer screening to date, both alone and in conjunction with serum biomarker screening using CA 125. The results of the published literature to date are inadequate to recommend the use of transvaginal US for ovarian cancer screening in postmenopausal patients without risk factors. A prior meta-analysis of 10 randomized trials, which employed US and/or serum CA 125 assessments for ovarian cancer screening failed to demonstrate a significant reduction in mortality as a result of screening [20]. The majority of trials that have investigated population based ovarian cancer screening aimed at accruing primarily average-risk postmenopausal patients. Across studies, the inclusion of high-risk patients was heterogeneous. The major clinical trials evaluating transvaginal US for ovarian cancer screening in average-risk patients are summarized below.

Jacobs et al [14] conducted a pilot randomized controlled trial in which postmenopausal patients were randomized to a control group (n = 10,977) or to annual screening with CA 125 (n = 10,958) for 3 years. Patients with a CA 125 >30 U/mL were referred for US, which was initially done via transabdominal scanning, and subsequently via the transvaginal approach, when this technique was more universally implemented. At US, ovarian volume ≥8.8 mL was designated as abnormal, whereas ovaries with normal volume but abnormal morphology were considered equivocal and followed with subsequent US. Patients with elevated CA 125 and abnormal US were referred for surgical consideration. An 86% compliance rate with at least one screening was achieved, establishing screening feasibility, with the positive predictive value (PPV) of screening with US being 21%. No significant difference in mortality from index cancers between the control and screened groups was observed [14].

Kobayashi et al [15] published a randomized controlled trial in which postmenopausal patients were randomized to a control group (n = 40,799) or to screening with US and CA 125 (n = 41,688). Patients with US studies who were considered normal were screened at 1 year and then rescreened after a 1 year interval for a total of 5 yearly screening evaluations. US was predominantly performed using a transvaginal approach. At US, ovaries were considered suspicious for malignancy if ovarian size was >4 cm and a complex morphology was apparent. Among the findings in this study, the number of screening-detected cancers (27 cancers detected in 41,688 patients, 0.06%) was found to be lower than for screening studies employing US and CA 125 conducted on the general population in the United States (0.54%) [12]. Whereas, a higher number of stage I cancers were detected in the screened group (63%) compared to the control group (38%), suggesting a shift in stage distribution with screening, this did not reach statistical significance [15].

van Nagell et al [19] published long-term results from a single-arm screening trial of annual transvaginal US conducted at the University of Kentucky designed to estimate the effect of screening on stage at detection and long-term ovarian cancer–specific survival. Eligibility included asymptomatic patients ≥50 years of age and patients ≥25 years of age with a documented family history of ovarian cancer. Patients with abnormal screens underwent tumor morphology indexing, serum biomarker analysis, and surgery. Based upon the study results, 22% had a family history of ovarian cancer, thus presumably the majority of the study cohort comprised average-risk postmenopausal patients. After a mean follow-up of 5.8 years, 70% of screen-detected cancers were stage I or II at diagnosis (compared with 27% of observed controls), and 5-year ovarian cancer–specific survival was 75% (compared with 54% for observed controls). Notably, this study design, with no control group and with a mixed-risk population, was subject to epidemiologic

biases. Importantly, a reduction in mortality has not been corroborated by randomized controlled trials employing transvaginal US for screening [12].

Buys et al [12] published results of the United States Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial in 2011, a randomized controlled trial in which postmenopausal patients were randomized to a control group (n = 39,111) or annual screening (n = 39,105) with CA 125 for 6 years and transvaginal US for 4 years. Participants were followed up for a maximum of 13 years (median [range], 12.4 years [10.9-13.0 years]) for cancer diagnoses and death. The main outcome measure was mortality from ovarian cancer, including primary peritoneal and fallopian tube cancers, with secondary outcomes including ovarian cancer incidence and complications associated with screening examinations and diagnostic procedures. US results were considered abnormal if ovarian or ovarian cyst volume was >10 mL or if intraovarian lesions demonstrated solid projections into cysts or mixed solid and cystic components [12]. Partridge et al [21] published results of the first 4 screening rounds from this trial in 2009, demonstrating a low PPV (range 1%-1.3%) for the screened group, with a predominance of late-stage cancers detected. In the final analysis, Buys et al [12] found no significant shift in stage distribution and no statistically significant reduction in ovarian cancer mortality. Of the 3,285 patients with false-positive results, 1,080 (33%) underwent surgical follow-up, with 163 (15%) of these patients experiencing a major complication, indicating that, for patients at average risk for ovarian cancer, screening increased both invasive medical procedures and associated harm [12].

Lu et al [16] reported results from a single-arm prospective trial of ovarian cancer screening evaluating a 2-stage ovarian cancer screening strategy that incorporated changes of CA 125 over time and age to estimate the risk of ovarian cancer in 4,051 postmenopausal patients using a Risk of Ovarian Cancer Algorithm (ROCA) score based on serum CA 125 measurements. In this study, patients with ROCA scores indicating intermediate risk (risk of ovarian cancer between 1 in 2,000 and 1 in 500) had a repeat CA 125 assessment in 3 months, and patients with ROCA scores indicating elevated risk (>1 in 500) were referred for transvaginal US and gynecologic oncology consultation. After 11 years of follow-up, 10 patients underwent surgery on the basis of transvaginal US, with 4 invasive ovarian cancers (1 with stage IA disease, 2 with stage IC disease, and 1 with stage IIB disease), 2 ovarian tumors of low malignant potential (both stage IA), 1 endometrial cancer (stage I), and 3 benign ovarian tumors. These results demonstrated a PPV of 40% for detecting invasive ovarian cancer and a specificity of 99.9%, indicating that the 2-step screening strategy using CA 125 and ROCA calculation achieved high specificity with few false-positive results [16]. All 4 patients with invasive ovarian cancer were enrolled in the study for at least 3 years and had low-risk annual CA 125 test values before rising CA 125 levels, supporting the concept that serial assessment of biomarkers over time might be a more useful screening tool than single value assessments such as those used in the PLCO trial, and that serial assessments might improve screening PPV and specificity. Notably, the sensitivity of this technique and the effect of this strategy on decreasing mortality from ovarian cancer was not evaluated as part of this trial.

The United Kingdom Collaborative Trial of Ovarian Cancer Screening was a randomized controlled trial designed to assess the effect of screening on mortality [13,17]. Over 200,000 postmenopausal patients were randomized to either a control group, multimodal screening (ie, annual CA 125 with transvaginal US as a follow-up test), or annual transvaginal US alone, with this study being the largest randomized controlled trial of ovarian cancer screening to date. US results were considered abnormal if ovaries demonstrated a complex morphology or had simple cysts >60 mL or if ascites

was present [17]. CA 125 results were designated based on the ROCA algorithm described by Menon et al [18] in earlier work, using an algorithm incorporating patient age and CA 125 trends to dictate management. In 2009, Menon et al [17] published results of the prevalence screen, which demonstrated that the multimodal strategy was superior to US alone, resulting in sensitivity, specificity, and PPV values of 89.4%, 99.8%, and 43.3% compared to 84.9%, 98.2%, and 5.3%, respectively. In 2016, Jacobs et al [13] reported long-term study results for the final cohort, which included 101,299 patients in the control group, 50,624 patients in the multimodal screening group, and 50,623 patients in the US-only group. After a median follow-up of 11.1 years, there was evidence of a stage shift due to screening. Although only 26% of primary ovarian and peritoneal cancers were detected as stage I, II, or IIIa cancers in the control group, a significantly higher proportion were diagnosed at an early stage in the multimodal group (40%) but not in the US-only group (24%). The primary study outcome measure of ovarian cancer mortality reduction did not achieve statistical significance over the 14-year study period. A significant ovarian cancer mortality reduction (20%) in the multimodal group relative to the control group was demonstrated via a post hoc analysis when accounting for expected delayed mortality reductions. These results suggested that the difference in mortality between no screening and screening groups may increase with time and further follow-up.

Although these collective findings suggest a possible role for population screening with transvaginal US in conjunction with biomarkers that is worthy of further investigation, they demonstrate a lack of stage shift and mortality reduction with US-only screening. As such, the current evidence is inadequate to recommend the use of transvaginal US for ovarian cancer screening in postmenopausal patients without risk factors, for whom screening with transvaginal US is usually not helpful.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.

The goal of ovarian cancer screening is early detection of ovarian cancer before it is detected clinically and before the onset of locally advanced or metastatic disease. Appropriate and effective imaging for ovarian cancer screening can confirm the presence of ovarian cancer at an earlier stage than via clinical assessment, thereby guiding management. The expected outcome for effective ovarian cancer screening is decreased burden of disease.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
A. CT abdomen and pelvis with IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis with IV contrast for ovarian cancer screening in premenopausal patients without risk factors.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
B. CT abdomen and pelvis without and with IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis without and with IV contrast for ovarian cancer screening in premenopausal patients without risk factors.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
C. CT abdomen and pelvis without IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis without IV contrast for ovarian cancer screening in premenopausal patients without risk factors.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
D. FDG-PET/CT skull base to mid-thigh

There is no relevant literature to support the use of FDG-PET/CT from the skull base to mid-thigh for ovarian cancer screening in premenopausal patients without risk factors.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
E. MRI pelvis without and with IV contrast

There is no relevant literature to support the use of MRI of the pelvis without and with IV contrast for ovarian cancer screening in premenopausal patients without risk factors.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
F. MRI pelvis without IV contrast

There is no relevant literature to support the use of MRI of the pelvis without IV contrast for ovarian cancer screening in premenopausal patients without risk factors.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
G. US color Doppler ovaries

There is no relevant literature to support the use of color Doppler US of the ovaries for ovarian cancer screening in premenopausal patients without risk factors.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
H. US pelvis transabdominal

There is no relevant literature to support the use of transabdominal US of the pelvis for ovarian cancer screening in premenopausal patients without risk factors. Most studies discussed in this document have addressed the use of transvaginal US for ovarian cancer screening in average-risk postmenopausal patients [12-19]. In general, transabdominal US should be reserved for patients in whom transvaginal US is not desired, not technically feasible, or as an adjunct to transvaginal US.

Variant 2: Adult. Ovarian cancer screening. Premenopausal. Average risk.
I. US pelvis transvaginal

There is no relevant literature to support the use of transvaginal US of the pelvis for ovarian cancer screening in premenopausal patients without risk factors.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.

The goal of ovarian cancer screening is early detection of ovarian cancer before it is detected clinically and before the onset of locally advanced or metastatic disease. Appropriate and effective imaging for ovarian cancer screening can confirm the presence of ovarian cancer at an earlier stage than via clinical assessment, thereby guiding management. The expected outcome for effective ovarian cancer screening is decreased burden of disease.

"High risk" is defined as personal or family history of breast or ovarian cancer, known or suspected genetic predisposition. These recommendations also apply for evaluation of patients tested and found to have elevated CA 125 as an initial step of screening.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
A. CT abdomen and pelvis with IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis with IV contrast for ovarian cancer screening in high-risk premenopausal patients.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
B. CT abdomen and pelvis without and with IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis without and

with IV contrast for ovarian cancer screening in high-risk premenopausal patients.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
C. CT abdomen and pelvis without IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis without IV contrast for ovarian cancer screening in high-risk premenopausal patients.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
D. FDG-PET/CT skull base to mid-thigh

There is no relevant literature to support the use of FDG-PET/CT from the skull base to mid-thigh for ovarian cancer screening in high-risk premenopausal patients.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
E. MRI pelvis without and with IV contrast

There is no relevant literature to support the use of MRI of the pelvis without and with IV contrast for ovarian cancer screening in high-risk premenopausal patients.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
F. MRI pelvis without IV contrast

There is no relevant literature to support the use of MRI of the pelvis without IV contrast for ovarian cancer screening in high-risk premenopausal patients.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
G. US color Doppler ovaries

Most studies discussed in this document have addressed the use of transvaginal US for ovarian cancer screening in average-risk postmenopausal patients [12-19]. Across these studies, the inclusion of high-risk patients has been heterogeneous. Although there has been a lack of methodologic detail to confirm the explicit benefits of color Doppler US of the ovaries, Doppler assessment of the ovaries is performed as part of routine transabdominal and transvaginal US studies. As such, it may be useful for select high-risk premenopausal patients (eg, those who defer or decline risk-reducing salpingo-oophorectomy) when used for these indications.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
H. US pelvis transabdominal

Most studies discussed in this document have addressed the use of transvaginal US for ovarian cancer screening in average-risk postmenopausal patients [12-19]. In general, transabdominal US should be reserved for patients in whom transvaginal US is not desired, not technically feasible, or as an adjunct to transvaginal US. As such, it may be useful for select high-risk premenopausal patients (eg, those who defer or decline risk-reducing salpingo-oophorectomy) when used for these indications.

Variant 3: Adult. Ovarian cancer screening. Premenopausal. High risk.
I. US pelvis transvaginal

Randomized controlled trials analogous in scale to those in average-risk populations have not been conducted in uniformly high-risk populations. Those studies that have been described are relatively small in sample size and most include a combination both of premenopausal and postmenopausal patients at high risk [22-25].

The largest study to date is the United Kingdom Familial Ovarian Cancer Screening Study, a single-

arm multisite prospective study of 3,563 premenopausal and postmenopausal patients with a lifetime risk of ovarian cancer ≥10% based on family history or known predisposing genetic mutation. The median participant age at study enrollment was 44.6 years (range 35-81 years)—thus, the assumption that the majority of high-risk patients in this study were premenopausal [26]. Patients in the study were followed over a mean of 3.2 years with a combination of annual transvaginal US and serum CA 125 measurements. The sensitivity of detection of incident ovarian/fallopian tube cancers in the study was 81.3% to 87.5%, depending on whether occult cancers detected at risk-reducing salpingo-oophorectomy were considered false-negatives or true positives. The PPV was 25.5%. Of the 13 incident cancers in the study, 4 (31%) were stage I or stage II. Of note, patients who had not undergone screening within 1 year of their diagnosis were more likely to have stage IIIc or higher cancer compared with patients who had received screening within the past year. These findings highlighted the importance of strict screening adherence, and as a result the screening frequency for phase II of the trial was reduced to 4 months.

In the phase II of this study, patients underwent screening with CA 125, interpreted using the ROCA, with transvaginal US performed annually if ROCA results were normal or within 2 months of an abnormal ROCA result [27]. Risk-reducing salpingo-oophorectomy was encouraged throughout the study. The International Federation of Gynecology and Obstetrics stage and postsurgery zero residual disease rates in ovarian cancer and fallopian tube cancer diagnosed during and <365 days from the end of screening were compared with those diagnosed >365 days after screening ended.

Data from the evaluation of 4,348 patients was analyzed, with a median follow up time of 4.8 years.

Nineteen patients were diagnosed with invasive ovarian or fallopian tube cancer within 1 year before screening, with 13 diagnoses screen-detected and 6 being occult and confirmed at risk-reducing salpingo-oophorectomy. No symptomatic interval cancers occurred. Ten (52.6%) of the total 19 diagnoses were stage I to II ovarian or fallopian tube cancers. Of the 13 screen-detected cancers, 5 (38.5%) were stage I to II. Of the 6 occult cancers, 5 (83.3%) were stage I to II (confidence interval [CI] 35.9%-99.6%). Seven (36.8%) of the 19 cancers diagnosed <1 year after prior screening were stage IIIb or IV ([CI 16.3%-61.6%) compared with 17 (94.4%) of 18 cancers diagnosed >1 year after screening ended, a difference that was statistically significant (CI, 72.7%-99.9%, *P* < .001) [27]. Eighteen (94.8%) of 19 cancers diagnosed <1 year after prior screening had zero residual disease (with lower surgical complexity, *P* = .16; CI, 74.0%-99.9%) compared with 13 (72.2%) of 18 cancers subsequently diagnosed (CI 46.5%-90.3%; *P* = .09). Modeled sensitivity, PPV, and negative predictive value (NPV) for ovarian or fallopian tube cancer detection within 1 year were 94.7%, 10.8%, and 100%, respectively [27]. These results suggest that in a high-risk population, screening may be useful, given its sensitivity and evidence for significant stage shift, in particular for those patients those who defer or decline risk-reducing salpingo-oophorectomy.

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.

The goal of ovarian cancer screening is early detection of ovarian cancer before it is detected clinically and before the onset of locally advanced or metastatic disease. Appropriate and effective imaging for ovarian cancer screening can confirm the presence of ovarian cancer at an earlier stage than via clinical assessment, thereby guiding management. The expected outcome for effective ovarian cancer screening is decreased burden of disease.

"High risk" is defined as personal or family history of breast or ovarian cancer, known or suspected

genetic predisposition. These recommendations also apply for evaluation of patients tested and found to have elevated CA 125 as an initial step of screening.

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
A. CT abdomen and pelvis with IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis with IV contrast for ovarian cancer screening in high-risk postmenopausal patients. Although CT is routinely used for ovarian cancer staging, its limited ability to evaluate the adnexae and accurately distinguish between benign and malignant ovarian lesions makes it an impractical screening tool in this setting. In a prior study of 2,869 postmenopausal patients undergoing CT screening colonography, in whom 118 (4.1%) were found to have incidentally detected adnexal lesions, no ovarian cancers were identified in those patients who underwent further workup with surgical resection. Moreover, 4 patients in the study cohort who subsequently developed ovarian cancer were noted to have had a prior negative CT examination [11].

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
B. CT abdomen and pelvis without and with IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis without IV contrast for ovarian cancer screening in high-risk postmenopausal patients. Although CT is routinely used for ovarian cancer staging, its limited ability to evaluate the adnexae and accurately distinguish between benign and malignant ovarian lesions makes it an impractical screening tool in this setting. In a prior study of 2,869 postmenopausal patients undergoing CT screening colonography, in whom 118 (4.1%) were found to have incidentally detected adnexal lesions, no ovarian cancers were identified in those patients who underwent further workup with surgical resection. Moreover, 4 patients in the study cohort who subsequently developed ovarian cancer were noted to have had a prior negative CT examination [11].

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
C. CT abdomen and pelvis without IV contrast

There is no relevant literature to support the use of CT of the abdomen and pelvis without IV contrast for ovarian cancer screening in high-risk postmenopausal patients. Although CT is routinely used for ovarian cancer staging, its limited ability to evaluate the adnexae and accurately distinguish between benign and malignant ovarian lesions makes it an impractical screening tool in this setting. In a prior study of 2,869 postmenopausal patients undergoing CT screening colonography, in whom 118 (4.1%) were found to have incidentally detected adnexal lesions, no ovarian cancers were identified in those patients who underwent further workup with surgical resection. Moreover, 4 patients in the study cohort who subsequently developed ovarian cancer were noted to have had a prior negative CT examination [11].

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
D. FDG-PET/CT skull base to mid-thigh

FDG-PET/CT is a useful imaging modality for the staging of cancer and detection of cancer recurrence. However, there is no relevant literature to support the use of FDG-PET/CT from the skull base to mid-thigh for ovarian cancer screening in high-risk postmenopausal patients.

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
E. MRI pelvis without and with IV contrast

There is no relevant literature to support the use of MRI of the pelvis without and with IV contrast for ovarian cancer screening in high-risk postmenopausal patients. MRI is a useful imaging

modality for the characterization of indeterminate mass detected on US [10]. However, it has not been used for population-based screening. given its unconfirmed benefit in this setting.

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
F. MRI pelvis without IV contrast

There is no relevant literature to support the use of MRI of the pelvis without and with IV contrast for ovarian cancer screening in high-risk postmenopausal patients. MRI is a useful imaging modality for the characterization of indeterminate mass detected on US [10]. However, it has not been used for population-based screening given its unconfirmed benefit in this setting.

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
G. US color Doppler ovaries

Most studies discussed in this document have addressed the use of transvaginal US for ovarian cancer screening in average-risk postmenopausal patients [12-19]. Across these studies, the inclusion of high-risk patients has been heterogeneous. Although there has been a lack of methodologic detail to confirm the explicit benefits of color Doppler US of the ovaries, Doppler assessment of the ovaries is performed as part of routine transabdominal and transvaginal US studies. As such, it may be useful for select high-risk premenopausal patients (eg, those who defer or decline risk-reducing salpingo-oophorectomy) when used for these indications.

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
H. US pelvis transabdominal

Most studies discussed in this document have addressed the use of transvaginal US for ovarian cancer screening in average-risk postmenopausal patients [12-19]. In general, transabdominal US should be reserved for patients in whom transvaginal US is not desired, not technically feasible, or as an adjunct to transvaginal US. As such, it may be useful for select high risk premenopausal patients (eg, those who defer or decline risk-reducing salpingo-oophorectomy) when used for these indications.

Variant 4: Adult. Ovarian cancer screening. Postmenopausal. High risk.
I. US pelvis transvaginal

Randomized controlled trials analogous to those in average-risk populations have not been conducted in definitively high-risk populations. Those studies that have been described are relatively small in sample size, most of which include a combination both of premenopausal and postmenopausal patients at high risk [22-25].

A secondary analysis of the PLCO data was performed by Lacey et al [28] to compare, within the screening arm, differences in screening outcomes (after the first 4 rounds of screening) between patients of varying risk for ovarian cancer. Patients were classified as average (n = 22,687), moderate (n = 2,572), or high (n = 2,163) risk based on family history, or high risk due to a personal history of breast cancer (n = 1,038). Although the PPV of screening was marginally higher for patients in specified moderate- and high-risk groups compared to those at average risk (PPV of 1.3% and 1.6% in the moderate- and high-risk groups, respectively, compared to 0.7% in the average-risk group), the PPVs did not significantly differ across risk groups.

Lai et al [29] published a separate subgroup analysis of PLCO data to determine whether annual screening with pelvic US and serum CA 125 reduced ovarian cancer mortality in a subgroup of patients with a first-degree relative with breast or ovarian cancer. Analysis was performed to

compare overall mortality and disease specific mortality in the screening versus usual care arm. In patients diagnosed with ovarian cancer, stage distribution and survival were analyzed as a secondary endpoint [29]. Outcomes for 11,293 patients in the screening group and 11,062 patients in the control group were compared, with subjects followed for a minimum of 10 years. As seen in the parent PLCO study, no significant difference in ovarian cancer mortality was observed between the screening and control groups. The secondary endpoints, however, showed notable differences. Significantly fewer patients were diagnosed with advanced stage disease in the screening, arm and survival was significantly improved (relative risk, 0.66, 95% CI, 0.47-0.93).

The largest study to date is the United Kingdom Familial Ovarian Cancer Screening Study, a single-arm multisite prospective study of 3,563 premenopausal and postmenopausal patients with a lifetime risk of ovarian cancer ≥10% based on family history or known predisposing genetic mutation. The median participant age at study enrollment was 44.6 years of age (range 35-81 years)—thus, the assumption that the majority of high-risk patients in this study were premenopausal [26]. Patients in the study were followed over a mean of 3.2 years with a combination of annual transvaginal US and serum CA 125 measurements. The sensitivity of detection of incident ovarian/fallopian tube cancers in the study was 81.3% to 87.5%, depending on whether occult cancers detected at risk-reducing salpingo-oophorectomy were considered false-negatives or true positives. The PPV was 25.5%. Of the 13 incident cancers in the study, 4 (31%) were stage I or stage II. Of note, patients who had not undergone screening within 1 year of their diagnosis were more likely to have stage IIIc or higher cancer compared with patients who had received screening within the past year. These findings highlighted the importance of strict screening adherence, and as a result, the screening frequency for phase II of the trial was reduced to 4 months.

In the phase II of this study, patients underwent screening with CA 125, interpreted using the ROCA, with transvaginal US performed annually if ROCA results were normal or within 2 months of an abnormal ROCA result [27]. Risk-reducing salpingo-oophorectomy was encouraged throughout the study. The International Federation of Gynecology and Obstetrics stage and postsurgery zero residual disease rates in ovarian cancer and fallopian tube cancer diagnosed during and <365 days from the end of screening were compared with those diagnosed >365 days after screening ended.

Data from the evaluation of 4,348 patients was analyzed, with a median follow up time of 4.8 years. Nineteen patients were diagnosed with invasive ovarian or fallopian tube cancer within 1 year of prior screening, with 13 diagnoses screen-detected and 6 being occult and confirmed at risk-reducing salpingo-oophorectomy. No symptomatic interval cancers occurred. Ten (52.6%) of the total 19 diagnoses were stage I to II ovarian or fallopian tube cancers. Of the 13 screen-detected cancers, 5 (38.5%) were stage I to II. Of the 6 occult cancers, 5 (83.3%) were stage I to II (CI, 35.9%-99.6%). Seven (36.8%) of the 19 cancers diagnosed <1 year after prior screening were stage IIIb or IV (CI 16.3%-61.6%) compared with 17 (94.4%) of 18 cancers diagnosed >1 year after screening ended, a difference that was statistically significant (CI 72.7%-99.9%, $P < .001$) [27]. Eighteen (94.8%) of 19 cancers diagnosed <1 year after prior screening had zero residual disease (with lower surgical complexity, $P = .16$; CI 74.0%-99.9%) compared with 13 (72.2%) of 18 cancers subsequently diagnosed (CI 46.5%-90.3%; $P = .09$). Modeled sensitivity, PPV, and NPV for ovarian or fallopian tube cancer detection within 1 year were 94.7%, 10.8%, and 100%, respectively [27]. These results suggest that in a high-risk population, screening may be useful, given its sensitivity and evidence for significant stage shift, in particular for those patients those who defer or decline

risk-reducing salpingo-oophorectomy.

Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- **Variants 1 and 2:** For ovarian cancer screening in adult postmenopausal and premenopausal patients at average risk, screening with imaging is usually not appropriate. This includes screening with US color Doppler of the ovaries, transabdominal pelvic US, transvaginal pelvic US, MRI of the pelvis without and with IV contrast, MRI of the pelvis without IV contrast, CT of the abdomen and pelvis with IV contrast, CT of the abdomen and pelvis without IV contrast, CT of the abdomen and pelvis without and with IV contrast, and FDG PET/CT skull base to mid-thigh.
- **Variants 3 and 4:** For ovarian cancer screening in adult premenopausal and postmenopausal patients at high risk, defined as a personal or family history of breast or ovarian cancer, or known or suspected genetic predisposition, or in those tested and found to have elevated CA 125 as an initial step of screening, screening with transvaginal pelvic US may be appropriate, in particular for those patients who defer or decline risk-reducing salpingo-oophorectomy. Screening that includes transabdominal pelvic US may be appropriate given that transabdominal US is performed in those patients in whom transvaginal US is not desired, not technically feasible, or as an adjunct to transvaginal US. Screening that includes Doppler assessment of the ovaries may be appropriate because Doppler assessment of the ovaries is performed as part of routine transabdominal and transvaginal US studies. For ovarian cancer screening in adult premenopausal and postmenopausal patients at high risk, screening is usually not appropriate using MRI of the pelvis without and with IV contrast, MRI of the pelvis without IV contrast, CT of the abdomen and pelvis with IV contrast, CT of the abdomen and pelvis without IV contrast, CT of the abdomen and pelvis without and with IV contrast, or FDG PET/CT skull base to mid-thigh.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates the use of the current understanding of language inclusive of diversity in sex, intersex, gender, and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document.

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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Disclaimer

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical

condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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