Primary care prevention and cancer screening

Somayeh Moradpanah , MD

Quality health care for individuals includes two fundamental elements:

- appropriate treatment for current illness and appropriate preventive care to attempt to lessen future health decline.
- Preventive health care is an important aspect of medical practice, leading to significant improvements in overall health

Periodic "check-up"

- There are no strict guidelines for the optimal frequency of periodic visits, and there is no evidence on which to base optimal frequency recommendations .
- Annual examinations are not indicated for most younger patients, although people with chronic health issues (such as diabetes) warrant regular visits, with or without a periodic health maintenance visit, independent of age .

Periodic "check-up"

- In the absence of such indications, we suggest periodic health maintenance visits every three years for adult patients ≤49 years without chronic conditions, and annually for adults ≥50 years.
- For people who have no chronic conditions and rarely see a clinician, a periodic health evaluation visit may be the only opportunity to discuss preventive care
- **Cardiovascular risk assessment** — Patients aged ≥20 years should undergo cardiovascular risk assessment every three to five years

Hypertension

- Hypertension screening is recommended for adults ≥18 years of age .
- The optimal interval for screening for hypertension is not known.
- Most patients have their blood pressure checked at each primary care visit.
- The 2021 US Preventive Services Task Force (USPSTF) guidelines recommend hypertension screening every year for adults ≥40 years and for those who are at high risk for high blood pressure (eg, patients with mean daytime blood pressure 130 to 139/80 to 89 mmHg, those with overweight or obesity, and African American individuals) .

Hypertension

- Adults aged 18 to 39 years without elevated blood pressure (ie, <130/80 mmHg) and without cardiovascular disease risk factors should be rescreened every three to five years.
- The USPSTF recommends obtaining out-of-office blood pressure measurements to confirm a diagnosis of hypertension before starting treatment.

Hyperlipidemia

- ●We suggest that patients aged 17 to 21 years undergo one-time screening for hyperlipidemia with a non-fasting non-high-density lipoprotein (non-HDL) cholesterol; non-HDL cholesterol is the difference between total cholesterol and HDL cholesterol .
- ●For patients with a normal screen before age 21 who are also at high risk, we suggest screening for lipid abnormalities starting at age 25 for men and 35 for women.
- We consider patients at high risk if they have more than one risk factor (eg, diabetes, hypertension, smoking, family history) or a single risk factor that is severe (eg, several siblings with coronary heart disease in their 40s or a very heavy smoker).

Hyperlipidemia

- ●For patients with a normal screen before age 21 who are not at high risk, we suggest screening for lipid abnormalities starting at age 35 for men and 45 for women .
- In patients whose lipid measurements place them well below the threshold for treatment (including lifestyle modification or lifestyle modification plus pharmacologic therapy), we suggest repeating measurements every five years.

Hyperlipidemia

- In patients who have had multiple lipid screenings with acceptable measurements, we suggest stopping screening at age 65. Ongoing assessment of cardiovascular risk can be based upon other risk factors and earlier lipid levels.
- When a decision is made to screen lipids to assess cardiovascular risk, we suggest measuring the total cholesterol and HDL cholesterol rather than a complete lipid profile or other lipid marker or fractions. Testing for total cholesterol and HDL cholesterol does not require a fasting test .

- **Iron deficiency** – We do not routinely screen every adult for iron deficiency, but we do screen those at higher risk (eg, premenopausal women, particularly those with prior pregnancies or heavy menstrual periods, as well as individuals with conditions that might cause blood loss or iron malabsorption). The frequency of screening is also individualized; annual screening may be reasonable for those at the highest risk, such as a menstruating individual with heavy periods.
- ●**Hypothyroidism** – do screen individuals who are at increased risk for hypothyroidism, including those with goiter, history of autoimmune disease, previous radioactive iodine therapy, and/or head and neck irradiation, family history of thyroid disease, and use of medications that may impair thyroid function.

- **Vitamin D deficiency** – it is not necessary to perform broad-based screening of serum 25(OH)D levels in the general population.
- We do, however, screen those at high risk of vitamin D deficiency (eg, limited or no sunlight exposure, individuals with obesity, osteoporosis, malabsorption).
- ●**Glaucoma** – we suggest that individuals over age 40 undergo periodic comprehensive eye evaluations by an eye specialist to evaluate for glaucoma.

CANCER PREVENTION

- **General cancer prevention counseling** — A number of measures can be taken to prevent cancer, including:
- ●Avoidance of tobacco
- ●Being physically active
- ●Maintaining a healthy weight
- ●Eating a diet rich in fruits, vegetables, and whole grains and low in saturated/trans fat
- ●Limiting alcohol consumption
- ●Protecting against sexually transmitted infections (including receiving human papillomavirus [HPV] vaccination)
- ●Avoiding excess sun exposure

Screening for breast cancer: Strategies and recommendations

- Breast cancer is the most frequent type of non-skin cancer and the most frequent cause of cancer death in women worldwide.

Major factors used to determine a risk category, based on a patient's history, are:

- ●Personal history of breast, ovarian, tubal, or peritoneal cancer
- ●Family history of breast, ovarian, tubal, or peritoneal cancer
- ●Ancestry (eg, Ashkenazi Jewish) associated with *BRCA1* or *2* mutations
- ●Known carrier of a pathogenic mutation for a hereditary breast and ovarian cancer syndrome in self or relative
- ●Mammographic breast density
- ●Previous breast biopsy indicating high-risk lesion (eg, atypical hyperplasia)
- ●Age of menarche, age at first live birth, number of pregnancies, and menopausal status
- ●Radiotherapy to the chest between age 10 and 30 years

- Women who have none of these risk factors are usually considered at average risk , lifetime risk of being diagnosed with breast cancer estimated at 12.4 percent.
- The majority of women are at average risk (less than 15 percent lifetime risk) of developing breast cancer.
- In these women, age is the most important factor in the decision about when to be screened, because breast cancer incidence rises with age .

AVERAGE RISK: SCREENING

- Breast cancer incidence is quite low under the age of 40 years and then begins to rise as women age.
- The sensitivity and specificity of mammography are also age-dependent, being higher in older women than in younger women .
- Thus, in younger women, the risk of developing breast cancer over the succeeding 10 years is quite low, and the benefits of screening may not outweigh the costs, inconvenience, emotional stress, occasional direct physical harm, and potential for overtreatment as a result of screening .
- When counseling women on screening, we discuss the potential benefits and harms of breast cancer screening and encourage them to consider their own values and preferences. We support women in making a decision that is best for them.

AVERAGE RISK: SCREENING

- **Age under 40 years** — No screening guidelines recommend routine screening . the incidence of breast cancer is low, there are no randomized trials of breast cancer screening, and the performance characteristics of mammography are poor.
- **Age 40 to 49 years** — Many expert groups encourage shared decision-making for women in their 40s because of trade-offs between benefits and harms ; although, the United States Preventive Services Task Force revised preliminary 2023 recommendations suggest starting routine screening at age 40 while both the American Cancer Society and European screening guidelines recommend starting screening at age 45 years

AVERAGE RISK: SCREENING

- **Age 50 to 74 years** — We suggest breast cancer screening with mammography for average-risk women aged 50 to 74 years, consistent with all major United States and international groups . We typically screen every one to two years depending on an individual woman's risk factors and preference.
- Systematic reviews of multiple randomized trials over the past 50 years found that mammographic screening for women aged 50 to 70 years decreases the risk of breast cancer mortality;

AVERAGE RISK: SCREENING

- **Age 75 years and older** — We suggest that women age 75 years and older be offered screening only if their life expectancy is at least 10 years. For women in this age group who elect to be screened, mammography screening every two years is appropriate.
- There is not a clear upper age limit or ideal frequency for screening in healthy women, since the incidence of breast cancer remains high into the 80s, but the number of life-years saved will decrease with age .
- Screening mammography may be less beneficial in women age 75 years and older, although data from randomized trials for this age group are limited .

Screening modalities

- — Mammography (digital 2D, digital breast tomosynthesis [3D], or film) is the primary modality for breast cancer screening in average-risk women.
- Other radiologic techniques, including ultrasound and MRI, are reserved for further evaluation of findings on mammography or for screening of women at a higher risk for breast cancer.
- Breast examination by the clinician or by the patient is not recommended as the only screening method, and it is controversial as to whether clinician breast examination (CBE) or patient breast self-examination (BSE) are beneficial as an adjunct to mammography. It is important to educate women about breast awareness and to encourage women to report any breast concerns.

Mammography as preferred screening modality

- —mammography is the best-studied and the only imaging technique that has been shown to decrease breast cancer mortality as demonstrated in multiple randomized trials. However, it is important to know that, even in the best circumstances, mammography may miss up to 20 percent of underlying breast cancers .
- Mammography is available as screen-film mammography, digital mammography, and digital breast tomosynthesis (3D mammography) . The choice between them generally depends upon availability .

Mammography as preferred screening modality

- For women with dense breasts, digital mammography or digital breast tomosynthesis , if available , is preferred because of higher sensitivity; the sensitivity of mammography is inversely correlated with breast density, especially with older film techniques .
- Prior to the mammogram, it is helpful for women to know that compression of the breasts is transient but important to reduce motion artifact, improve image quality, and reduce the amount of radiation required.
- Individuals should also provide access to their prior mammograms for comparison if they go to a different mammography facility than they used previously

Other imaging modalities

- For average-risk , there is a lack of medical evidence to routinely recommend other imaging or screening with ultrasound, MRI, or newer imaging technologies . However, these technologies are useful as adjuncts to screening for certain higher-risk patients and as diagnostic, rather than screening, tools.
- ●Screening ultrasound is not recommended for screening average-risk women. Ultrasound has not been evaluated as a screening strategy to reduce breast cancer mortality in the average-risk population, including among women with dense breasts.
- Ultrasound is commonly used for diagnostic follow-up of an abnormality seen on screening mammography to clarify features of a potential lesion.
- ●Screening MRI is not recommended for average-risk women, according to supplemental screening MRI guidelines from the ACS . MRI performed in combination with mammography is used primarily to screen high-risk patients with >20 percent lifetime risk

Role of clinical breast examination

- — We suggest **not** performing CBE as part of **screening** of average-risk women; however, a diagnostic CBE remains an important part of the evaluation for women with breast complaints or abnormalities. evidence suggesting an increase in false-positive rates.
- Although there is expert consensus that CBE should **not** be the only screening method used, recommendations of major societies differ as to whether or not to include CBE as an adjunctive screening modality .
- WHO states that CBE may be an appropriate screening approach for women 50 to 69 years of age in low-resource settings with weak health systems .

Role of breast self-examination

- We suggest that average-risk women **not** perform BSE. Several studies have shown a lack of benefit and a higher rate of breast biopsies that showed benign disease with routine BSE.
- Women who nonetheless choose to perform BSE should receive careful instruction to differentiate normal tissue from suspicious lumps and understand that BSE is an adjunct, but not a substitute, for mammography. Women should be encouraged to bring abnormal breast findings promptly to the attention of their clinician.
- Although many expert groups do not encourage BSE, many do encourage educating women about breast self-awareness, general breast health, and the benefits and the limitations of BSE, as well as advising women to seek medical attention soon if they note concerning breast abnormalities .
- The WHO recommends BSE as a way to empower women and raise awareness among women at risk, rather than as a screening method .

Frequency of screening with mammography

- every one to two years based on patient preference
- annual screening is associated with more harms and costs than screening every two years, and the difference in absolute benefits between annual and biennial screening is small .
- While some data suggest benefit for annual screening for some women (eg, premenopausal), this benefit needs to be weighed against the increased risk of false-positive mammographic findings and overdiagnosis.
- Expert group recommendations for frequency of mammography screening vary between annual and every two years screening, depending mostly upon the patient’s age.

MODERATE RISK: SCREENING

- — For women with moderate risk (ie, approximately 15 to 20 percent lifetime risk of breast cancer), including :
- most women who have a family history of breast cancer in a first-degree relative but do not have a known genetic syndrome,
- we suggest that the same screening approach, including the age to begin mammography screening, and frequency of screening be used as for women at average risk.

MODERATE RISK: SCREENING

- While some have suggested that screening be initiated at an earlier age if a first-degree relative had premenopausal breast cancer, there are few high-quality data supporting this approach in the absence of a known genetic syndrome.
- Many experts suggest that in women at moderate risk, the decision to undergo supplemental screening (with either magnetic resonance imaging [MRI] or ultrasound in addition to mammography) should be determined after a discussion with the patient regarding personal preferences for known risks versus possible benefits, availability, and insurance coverage .

MODERATE RISK: SCREENING

- . Supplemental screening ultrasound may be more widely accessible and less expensive than supplemental MRI;
- We do not routinely suggest these adjunctive modalities for women at moderate risk, but if women are interested in them, we encourage them to engage in a shared decision-making discussion with their clinician.
- Recommendations for MRI in women with moderate risk are inconclusive.
- ACS advises that there is insufficient evidence to recommend for or against supplemental screening MRI as an adjunct to mammography in moderate-risk women

ACS recommendations for breast MRI screening as an adjunct to mammography

Recommend annual MRI screening (based on high risk of breast cancer and high sensitivity of MRI*)
BRCA mutation
First-degree relative of *BRCA* carrier, but untested
Lifetime risk >20 to 25% or greater, as defined by BRCAPRO or other models that are largely dependent on family history
Recommend annual MRI screening (based on high risk of breast cancer)
Radiation to chest between age 10 and 30 years
Li-Fraumeni syndrome and first-degree relatives
Cowden and Bannayan-Riley-Ruvalcaba syndromes and first-degree relatives
Insufficient evidence to recommend for or against MRI screening$^{\Delta}$
Lifetime risk 15 to 20%, as defined by BRCAPRO or other models that are largely dependent on family history
Lobular carcinoma in situ or atypical lobular hyperplasia
Atypical ductal hyperplasia
Heterogeneously or extremely dense breast on mammography
Women with a personal history of breast cancer, including ductal carcinoma in situ
Recommend against MRI screening (based on expert consensus opinion)
Women at <15% lifetime risk

HIGH RISK: SCREENING

- who have known *BRCA* or other susceptibility genes,
- those with a history of chest radiation prior to the age of 30,
- those with certain breast conditions such as atypical hyperplasia,
- and those with a calculated lifetime risk of developing breast cancer of greater than 20 percent

HIGH RISK: SCREENING

- For those with a calculated lifetime risk of breast cancer exceeding 20 percent, we suggest supplemental screening with MRI in addition to mammography, consistent with guidelines from major groups .
- A common approach is to perform each modality annually, staggered by six months , although the optimal screening interval is not determined and other centers may perform both examinations simultaneously. We also refer such patients for genetic counseling, if not already done, and to a high-risk clinic for consideration of risk reduction treatment

HIGH RISK: SCREENING

- The rationale for supplemental MRI is its higher sensitivity for the detection of breast cancer in high-risk populations than mammography or ultrasound; therefore, it is used for screening women who are at significantly high risk for the development of breast cancer . However, despite evidence that MRI can detect smaller cancers and more node-negative malignancies in high-risk women than other imaging modalities, there is no evidence for a reduction in mortality or improved disease-free survival from screening with MRI . Another drawback of supplemental MRI screening is potential false-positives.

breast cancer prevention

- For women who are at an increased risk for breast cancer, we agree with guidelines from the NCCN, the American Society of Clinical Oncology (ASCO), and the United States Preventive Services Task Force (USPSTF) and suggest endocrine therapy (tamoxifen, raloxifene, anastrozole, or exemestane) for breast cancer prevention . criteria are the same as those adopted by ASCO and include :
- ●Age of 35 years or older with a life expectancy of at least 10 years and one of the following:
- •A history of thoracic radiation administered prior to 30 years of age.
- •A history of lobular carcinoma in situ.
- •A ≥1.7 percent five-year risk for breast cancer.
- •Atypical hyperplasia

- Although mastectomy is an option to prevent breast cancer, it is only recommended in women with a pathogenic/likely pathogenic genetic mutation conferring a high risk for breast cancer, compelling family history, or possibly with prior thoracic radiation at <30 years of age .
- For those with *BRCA1* and *BRCA2* mutations who do not undergo mastectomy, limited retrospective data suggest a benefit with tamoxifen .
- There are no data on the use of either the selective estrogen receptor modulators (SERMs) or aromatase inhibitors (AIs) for breast cancer prevention in men.

Cervical cancer screening

- **Age <21** — We suggest **not** screening for cervical cancer in asymptomatic, immunocompetent patients, <21 years, regardless of the age of initiation of sexual activity .
- **Age 21 to 29** — In asymptomatic, immunocompetent patients, the age at which to initiate cervical cancer screening and which testing method (eg, Pap smear, primary HPV testing) is preferable is unclear and recommendations from expert groups vary. initiate cervical cancer screening at the age of 21 with cervical cytology every three years

Cervical cancer screening

- **Age 30 to 65** — We recommend continuing cervical cancer screening in all asymptomatic, immunocompetent patients with a cervix between the ages of 30 and 65.
- Any of the following strategies are acceptable for patients with all normal results in this age group :
- ●Primary HPV testing (with an FDA-approved test) every five years; or
- ●Co-testing (Pap and HPV testing) every five years; or
- ●Pap test alone every three years

Cervical cancer screening

- **Age >65 years**
- **If adequate prior and all normal screening** — We suggest **discontinuing** screening in average-risk patients over the age of 65 who have adequate prior screening (defined below) and no factors that warrant extended screening.
- Discontinuing screening is predicated upon meeting both of the following criteria:
- ●Having no history of cervical intraepithelial neoplasia (CIN) grade 2+ for the past 25 years **and**
- ●Having **adequate** prior screening, as defined by :
- •Two consecutive negative primary HPV tests within the past 10 years, with the most recent test within the previous five years **or**
- •Two consecutive negative co-tests (Pap and HPV testing) within the past 10 years, with the most recent test within the previous five years **or**
- •Three consecutive negative Pap tests within the past 10 years, with the most recent test within the previous three years

Ovarian cancer

- is not a highly prevalent disease. Worldwide, there are 300,000 new cases of ovarian cancer and 185,000 ovarian-cancer related deaths annually, with the highest incidence rates in developed countries .
- A genetic predisposition (eg, *BRCA1, BRCA2*, Lynch syndrome, or others) is known to be present in about 10 percent of patients with ovarian cancer.

SCREENING APPROACH

- **Family history** — A family history is essential to identifying patients with a potential hereditary (eg, familial) cancer syndrome.
- **High-risk family history** — should be referred to a genetic counselor. Genetic counseling includes a discussion of genetic screening for a possible hereditary cancer syndrome (eg, *BRCA1*, *BRCA2,* Lynch syndrome, and other mutations) . Patients who test positive for one of these syndromes may benefit from specific interventions such as risk-reducing BSO .

SCREENING APPROACH

- **Lower-risk family history** — A patient may have a history (eg, a remote family member with ovarian cancer, without evidence of a hereditary pattern) that increases risk to a lesser extent than a hereditary cancer syndrome.
- When there is a family history without evidence for a hereditary cancer syndrome, there is no evidence that screening is effective and screening is generally not advised.
- **Average-risk patients** — In asymptomatic women at average risk (without a genetic predisposition or family history of ovarian cancer), we recommend against screening for ovarian cancer . Based on the available data, there is no evidence that the benefits of screening for ovarian cancer outweigh the harms related to the adverse effects of following up on findings that turn out to be false positives .

Tests

- **Cancer antigen 125 (CA 125)** — CA 125, an ovarian cancer tumor marker, did not reduce mortality due to ovarian cancer when studied as a possible screening test in the randomized Prostate, Lung, Colon, Ovarian Cancer (PLCO) Cancer Screening Trial.
- **Transvaginal ultrasound (TVUS)** — In the aggregate, studies do not suggest that screening with TVUS reduces ovarian cancer mortality

Multimodal (CA 125 and TVUS) tests

- •**Average risk** – Did not reduce mortality in the general population.
- **High risk** – Studies of concurrent testing with CA 125 and TVUS in high-risk patients are largely limited to observational studies and have found that most detected cancers (70 to 80 percent) are stage III or IV .
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- Women who had not been screened in the year before cancer diagnosis were more likely to have stage IIIC or higher cancer than women screened in the preceding year (86 versus 26 percent); detection of lower-stage disease in women who adhered to screening has led to a decision to decrease the screening interval to four months for the next phase of the study.

Colorectal cancer

- No risk factors – We recommend that average-risk patients aged 45 and older be screened for colorectal cancer.

We suggest that screening be continued until the life expectancy for an individual patient is estimated as less than 10 years.

For most patients, it is reasonable to stop screening at age 75 years or 85 years at the latest. One-time screening with colonoscopy (to age 83) or sigmoidoscopy (to age 84) is advised for adults who have never been screened for colorectal cancer.

Colorectal cancer

- The decision about which option to select should be made between the patient and clinician, weighing factors of effectiveness, safety, cost, and availability of the screening tests.
- ●Family history of colorectal cancer.
- ●Familial adenomatous polyposis.
- ●Lynch syndrome.
- ●Peutz-Jeghers syndrome.
- ●Inflammatory bowel disease