

Breast Cancer Screening in the Average Risk Woman, ANMC

Background

Cancer remains the leading cause of death among Alaska Native (AN) people. During the most recent 5 year period for which we have data (2014–2018), there were on average each year 480 new cases of cancer diagnosed and 183 cancer deaths. During the five-year period 2014–2018, there were 2,401 cases of invasive cancer diagnosed among AN people, which was an increase compared to the 2,123 diagnosed during the previous five-year period 2009–2013.

From 2014–2018, the most commonly diagnosed cancer among women was female breast (340 cases, 14% of all cancers). This pattern is identical to the previous five-year period (2009–2013) as well as the fifty-year period 1969–2018.

From the 1970s to mid-1990s, breast cancer incidence rates increased dramatically. In the 40 years between 1969 and 2008, the incidence of breast cancer among AN women tripled. However, since the mid-1990s there appears to have been no significant change in these rates. While AN breast cancer incidence rates were once much lower than USWs, breast cancer incidence rates are now similar to those among US White women (USW). Despite these gains, breast cancer is the leading cause of cancer in AN women, found in 139 per 100,000 (1969 – 2003), and is the second leading cause of cancer death AN among women.

While primary prevention played the major part in the recent trend, a 2017 study indicated that most AN women diagnosed with breast cancer within the AN Tribal Health System receive timely treatment after diagnosis. In contrast, a 2018 report found no improvements in survival from breast cancer despite an increase in the reported prevalence of breast cancer screening mammography from 62.2% (1991-1995) to 77.1% (2006- 2014) among women aged 50 to 74 years.

Overall, AI/ ANs have lower cancer incidence, but worse five- year survival outcomes, than non- Hispanic Whites (NHWs) for breast cancer. AI/ ANs are also more likely to present with late- stage, metastatic cancers, and this is particularly notable for cancers for which screening is available, including breast, colorectal, and prostate cancers. A 2018 study suggests that enrollment in the Indian Health System reduced the disparity between AI/ ANs and NHW with respect to late- stage cancer diagnoses compared to Medicare based care.

Cancers such as lung and breast can be viewed as an indicator of the rapid social, economic and environmental changes that Arctic populations, especially indigenous peoples, are experiencing. For breast cancer, genetic susceptibility may be an important risk factor, as a BRCA1 founder mutation has been found in the Greenlandic population, though not studied elsewhere in the Arctic. A 2014 study suggested that AN women may be exposed to types and concentrations of environmental chemicals that are different from other populations of women in the US. Studies of dichlorodiphenyltrichloroethane (DDT), or polychlorinated biphenyls (PCBs), have not demonstrated with any certainty that exposure to these chemicals results in increased risk of developing breast cancer.

Breast cancer rates are increasing in women 40-49 years of age while rates in older women have decreased. (JAMA 2023)

Primary prevention

The goal of screening for cancer is to detect preclinical disease in healthy, asymptomatic patients to prevent adverse outcomes, improve survival, and avoid the need for more intensive treatments. Screening tests have both benefits (eg, improved health outcomes) and adverse consequences (eg, cost, anxiety, inconvenience, false-positive results, and other test-specific harms such as overdiagnosis and overtreatment).

The following guideline will focus on breast cancer screening in the average risk woman. It will also allude to high risk women and provide resources for their management. (Appendix 1)

Risk factors:

The main factors for breast cancer are female sex (more than 99% of cases of breast cancer occur in women) and advancing age. Although other characteristics have been associated with an increased risk of breast cancer (Box 1), most women in whom invasive breast cancer is diagnosed do not have identifiable risk factors.

Health care providers periodically should assess breast cancer risk by reviewing the patient's history. Breast cancer risk assessment is based on a combination of the various factors that can affect risk (Box 1).

Initial assessment should elicit information about reproductive risk factors, results of prior biopsies, ionizing radiation exposure, and family history of cancer. Health care providers should identify cases of breast, ovarian, colon, prostate, pancreatic, and other types of germline mutation-associated cancer in first-degree, second-degree, and possibly third-degree relatives as well as the age of diagnosis. Women with a potentially increased risk of breast cancer based on initial history should have further risk assessment. (Appendix 1) Assessments can be conducted with one of the validated assessment tools available online, such as the Gail and other models.

'Breast self-awareness' vs breast self examination

'Breast self-awareness' is defined as a woman's awareness of the normal appearance and feel of her breasts. Breast self-examination is the inspection of a woman's breasts on a regular, repetitive basis for the purpose of detecting breast cancer. Unlike breast self-examination, 'breast self-awareness' does not include a recommendation for women to examine their breasts in a systematic way or on a routine basis. On the other hand, breast self-examination is not recommended in average-risk women because there is a risk of harm from false-positive test results and a lack of evidence of benefit. Average-risk women should be counseled about 'breast self-awareness' and encouraged to notify their health care provider if they experience a change.

Screening clinical breast examination

Screening clinical breast examination by a provider may be offered to asymptomatic, average-risk women in the context of an informed, shared decision-making approach that recognizes the uncertainty of additional benefits and the possibility of adverse consequences of clinical breast examination beyond screening mammography. If performed for screening, intervals of every 1–3 years for women aged 25–39 years and annually for women 40 years and older are reasonable. The clinical breast examination continues to be a recommended part of evaluation of high-risk women and women with symptoms.

When should screening with mammography begin?

Women at average risk of breast cancer should be offered screening mammography starting at age 40 years. Women at average risk of breast cancer should initiate screening mammography no earlier than age 40 years. If they have not initiated screening in their 40s, they should begin screening mammography by no later than age 50 years. The decision about the age to begin mammography screening should be made through a shared decision-making process. This discussion should include information about the potential benefits and harms.

How frequently should mammography be repeated?

Women at average risk of breast cancer should have screening mammography every 1 or 2 years based on an informed, shared decision-making process that includes a discussion of the benefits and harms of annual and biennial screening and incorporates patient values and preferences. Biennial screening mammography, particularly after age 55 years, is a reasonable option to reduce the frequency of harms,

as long as patient counseling includes a discussion that with decreased screening comes some reduction in benefits.

How about screening during pregnancy and lactation?

Rates of pregnancy and lactation are increasing in women over age 40. (CDC 2021)

The American College of Radiology states:

-Mammography is safe during pregnancy and breast cancer screening should be tailored to patient age and breast cancer risk.

-Pregnancy-associated breast cancer is increasing as more women delay childbearing into the fourth decade of life, and imaging of clinical symptoms should not be delayed.

-The fetal radiation dose from a 4-view mammogram is negligible at $<0.03\text{mGy}$.

-There is no contraindication to performing mammography during lactation.

-Because of the potential increased risk of breast cancer in this population, consider continue screening during lactation dependent upon the level of underlying risk and the expected duration of lactation.

Hence the decision about mammography screening after age 40 years during pregnancy and lactation should be made through a shared decision-making process. This discussion should include information about the potential benefits and harms.

When should screening mammography cease?

Women at average risk of breast cancer should continue screening mammography until at least age 75 years. Age alone should not be the basis to continue or discontinue screening. Beyond age 75 years, the decision to discontinue screening mammography should be based on a shared decision-making process informed by the woman's health status and longevity

Box 1

Box 1. Breast Cancer Risk Factors ↻

- Family history of breast cancer, ovarian cancer, or other hereditary breast and ovarian syndrome-associated cancer (eg, prostate cancer, pancreatic cancer)
- Known deleterious gene mutation
- Prior breast biopsy with specific pathology
 - Atypical hyperplasia (lobular or ductal)
 - Lobular carcinoma in situ
- Early menarche
- Late menopause
- Nulliparity
- Prolonged interval between menarche and first pregnancy
- Menopausal hormone therapy with estrogen and progestin (decreased risk with estrogen alone)
- Not breastfeeding
- Increasing age
- Certain ethnicities (eg, increased risk of *BRCA* mutation in Ashkenazi Jewish women)
- Higher body mass index
- Alcohol consumption
- Smoking
- Dense breasts on mammography
- Prior exposure to high-dose therapeutic chest irradiation in young women (10–30 years old)

(ACOG Practice Bulletin No. 179, 2017)

Recommendations

The following recommendations assume the patient does not have either known familial risk factors either by history taking / BRAC testing; or other criteria from one of the electronic risk assessments which place them in a different screening category.

- Women at average risk of breast cancer should be offered screening mammography starting at age 40 years. Women at average risk of breast cancer should initiate screening mammography no earlier than age 40 years. If they have not initiated screening in their 40s, they should begin screening mammography by no later than age 50 years. The decision about the age to begin mammography screening should be made through a shared decision-making process. This discussion should include information about the potential benefits and harms.

- Women at average risk of breast cancer should have screening mammography every 1 or 2 years based on an informed, shared decision-making process that includes a discussion of the benefits and harms of annual and biennial screening and incorporates patient values and preferences. Biennial screening mammography, particularly after age 55 years, is a reasonable option to reduce the frequency of harms, as long as patient counseling includes a discussion that with decreased screening comes some reduction in benefits.
- Mammography is safe during pregnancy and lactation and breast cancer screening should be tailored to patient age and breast cancer risk.
- Women at average risk of breast cancer should continue screening mammography until at least age 75 years. Age alone should not be the basis to continue or discontinue screening. Beyond age 75 years, the decision to discontinue screening mammography should be based on a shared decision making process informed by the woman’s health status and longevity.
- Screening clinical breast examination by a provider may be offered to asymptomatic, average-risk women in the context of an informed, shared decision-making approach that recognizes the uncertainty of additional benefits and the possibility of adverse consequences of clinical breast examination beyond screening mammography. If performed for screening, intervals of every 1–3 years for women aged 25–39 years and annually for women aged 40 years and older are reasonable. The clinical breast examination continues to be a recommended part of evaluation of high-risk women and women with symptoms.
- Breast self-examination is not recommended in average-risk women because there is a risk of harm from false-positive test results and a lack of evidence of benefit.
- Average-risk women should be counseled about ‘breast self-awareness’ and encouraged to notify their health care provider if they experience a change. ‘Breast self-awareness’ is defined as a woman’s awareness of the normal appearance and feel of her breasts.
- For recommendations from other benchmark organizations, please see Appendix 2

Appendix 1: Reproductive Risk Factors

Certain reproductive factors influence breast cancer risk, particularly the risk of hormone receptor-positive breast cancer. A systematic review indicates that nulliparity and longer intervals between menarche and age at first birth are associated with an increased risk of hormone receptor-positive breast cancer. Other

less consistently reported reproductive risk factors for breast cancer include older age at first birth, older age at menopause, and younger age at menarche. In contrast, certain reproductive factors appear to decrease the risk of breast cancer. Parity appears to decrease the risk of hormone receptor-positive breast cancer, and breastfeeding is associated with a reduced risk of hormone receptor-positive breast cancer and triple-negative breast cancer (ie, estrogen-receptor negative, progesterone negative, and *ERBB2*-negative [formerly *HER2/Neu*-negative]).

Menopausal Hormone Therapy

Breast cancer risk appears to differ between postmenopausal women who use combined hormonal therapy and those who use estrogen therapy alone. In the Women's Health Initiative randomized controlled trial, postmenopausal women taking estrogen and progestin had higher breast cancer risk during the intervention and early postintervention parts of the study. In postmenopausal women who previously had a hysterectomy and were randomized to receive estrogen alone or placebo, breast cancer risk did not appear increased.

Familial Risk Factors

Family history of breast cancer, ovarian cancer (including fallopian tube cancer and primary peritoneal cancer), and other types of germline mutation-associated cancer (eg, prostate and pancreatic) are associated with an increased risk of breast cancer. For family members with cancer, breast cancer onset at a young age is associated with an increased risk of the presence of a germline mutation.

For more information:

ACOG Practice Bulletin No. 103, *Hereditary Breast and Ovarian Cancer Syndrome*.

Breast Disorders

Atypical ductal hyperplasia, atypical lobular hyperplasia, and lobular carcinoma in situ are typically found incidentally upon histologic evaluation of abnormal mammography findings or breast masses. Women with these diagnoses have a four-fold risk of subsequent invasive cancer in the affected and contralateral breasts, with some studies reporting a cumulative incidence of breast cancer approaching 30% at 25 years of follow-up.

For more information:

Practice Bulletin No. 164, *Diagnosis and Management of Benign Breast Disorders*.

Breast Density

Women with dense breasts diagnosed by mammography have a modestly increased risk of breast cancer. Mammography has reduced sensitivity to detect breast cancer in women with dense breasts. Breast cancer screening in women with dense breasts is beyond the scope of this document.

For more information:

-American College of Radiology ACR Appropriateness Criteria® Supplemental Breast Cancer Screening Based on Breast Density

-ACOG Committee Opinion No. 625, *Management of Women With Dense Breasts Diagnosed by Mammography*

Ionizing Radiation

Women treated for Hodgkin lymphoma with therapeutic chest radiation therapy between the ages of 10 years and 30 years (and possibly as late as age 45 years) are at an increased risk of breast cancer. Girls who are treated between the ages of 10 years and 14 years appear to be at greatest risk of future development of breast cancer.

Appendix 2: Recommendations of Benchmark Organizations, 2023

Table 1. Recommendations for Breast Cancer Screening in Average-Risk Women ↻

	American College of Obstetricians and Gynecologists	U.S. Preventive Services Task Force	American Cancer Society	National Comprehensive Cancer Network
Clinical breast examination	May be offered* every 1–3 years for women aged 25–39 years and annually for women 40 years and older.	Insufficient evidence to recommend for or against. [†]	Does not recommend [‡]	Recommend every 1–3 years for women aged 25–39 years. Recommend annually for women 40 years and older.
Mammography initiation age	Offer starting at age 40 years. [§] Initiate at ages 40–49 years after counseling, if patient desires. Recommend by no later than age 50 years if patient has not already initiated.	Recommend at age 50 years. Age 40–49 years: The decision to start screening mammography in women before age 50 years should be an individual one. [‡]	Offer at ages 40–45 years. [‡] Recommend at age 45 years. [‡]	Recommend at age 40 years.
Mammography screening interval	Annual or biennial [§]	Biennial	Annual for women aged 40–54 years [‡] Biennial with the option to continue annual screening for women 55 years or older [‡]	Annual
Mammography stop age	Continue until age 75 years. Beyond age 75 years, the decision to discontinue should be based on a shared decision-making process that includes a discussion of the woman's health status and longevity.	The current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women 75 years and older. [‡]	When life expectancy is less than 10 years [‡]	When severe comorbidities limit life expectancy to 10 years or less

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