**GOAL**
To provide guidance on the appropriate use of screening tools for breast cancer and to help physicians, clinicians and women make informed decisions about screening for breast cancer

**TARGET POPULATION**
Asymptomatic women of all ages

**EXCLUSIONS**
Women with signs and symptoms suggesting breast cancer

Women with a history of ductal carcinoma in situ or invasive breast cancer

Men

# RECOMMENDATIONS

## RISK ASSESSMENT

An assessment of risk for breast cancer should occur for all women. Consider a woman's age, medical history, maternal and paternal family history, and other associated risks in determining her breast cancer screening needs.

The guideline recommendations are categorized as follows:



## AVERAGE RISK POPULATION

### *BENEFITS AND RISKS OF SCREENING*

Discuss the benefits and risks of screening specific to each age group. Refer to Appendix A – Resources

## MAMMOGRAPHY

| Age Group | Mammography Screening Recommendation | Interval |
|---|---|---|
| 39 years and under | Screening with mammography is not recommended | |
| 40 to 49 years | The balance of benefits and risks is not great enough to recommend routine screening. Consider woman's preference whether to start screening | For those choosing to be screened, the optimal interval is considered to be one year |
| 50 to 74 years | Screening recommended | Screen every 2 years |
| 75 years and older | Consider individual health factors and woman's preference to continue screening | |

Women with surgery for breast augmentation, breast reduction, sex-reassignment: Follow above recommendations for mammographic screening in the average risk population. Note presence of implants in history section of mammography requisition form.

**PRACTICE POINT**

*Mammography is the recommended method of screening for women in the average risk population*

## CLINICAL BREAST EXAMINATION (CBE)

CBE should not be considered as a replacement for mammography screening.

CBE should be considered as part of the physical examination and used as a teaching opportunity to discuss breast health.

## BREAST AWARENESS

Encourage women to report changes in their breasts; in particular, nipple discharge, rash on nipples, inversion, dimpling or new mass in the breast or axilla.

## BREAST SELF-EXAMINATION (BSE)

BSE is not recommended as a screening method.

## OTHER TECHNOLOGY

Magnetic Resonance Imaging: MRI should not be used for screening the average risk population. MRI may be used in specific circumstances as determined by a radiologist.

Ultrasound: Ultrasound should not be used for screening the average risk population.

Tomosynthesis: Tomosynthesis should not be ordered for screening. Tomosynthesis may be used in specific circumstances as determined by a radiologist.

Thermography: Thermography should not be used for the detection of breast cancer.

**PRACTICE POINT**

*The majority (80% +) of breast cancer occurs in women in the average risk population*

# HIGH RISK POPULATION

## *WOMEN REQUIRING MORE INTENSIVE SCREENING*

Women with one or two first degree relatives with invasive breast cancer, but who do not meet the criteria for referral to Medical Genetics:

- Annual mammography starting 5 to 10 years younger than the youngest case in the family, but no earlier than age 25 and no later than age 40
- Annual clinical breast examination starting at age 25

Women with a breast biopsy showing atypical hyperplasia or lobular carcinoma in situ and following surgical management to rule out invasive carcinoma:

- Annual mammography
- Annual clinical breast examination

Women with a history of chest wall radiation (i.e., mantle radiation for treatment of Hodgkin's lymphoma) at age 30 or younger:

- Annual mammography and breast screening MRI starting 5 to 10 years after radiation given, but starting no earlier than age 25 and no later than age 40
- Annual clinical breast examination

## *CRITERIA FOR REFERRAL TO MEDICAL GENETICS*

Women with families **(maternal or paternal)** meeting the criteria below should be referred to Medical Genetics in Edmonton or Calgary for potential counselling +/- genetic testing.

- Multiple individuals with breast and/or ovarian* cancer (e.g., three or more cases in two or more generations, at least one case onset under the age of 50), related to each other
- Bilateral primary breast cancer, first onset age 50 or younger
- Breast cancer at age 35 or younger
- Breast cancer that is hormone receptor negative and HER2 negative (a.k.a. triple negative), age 60 or younger
- Primary breast and primary ovarian cancer in the same individual
- Male breast cancer, age 65 or younger, or at any age with close family history of breast cancer
- Breast or ovarian cancer in a family with Ashkenazi Jewish heritage
- BRCA1 or BRCA2 mutation in the family

**serous epithelial cancer of the ovaries, fallopian tube cancer or primary peritoneal cancer*

Follow recommendations from Medical Genetics regarding screening and risk reduction.

For eligible women who decline or are unable to attend counseling, follow the recommendations for women with one or two first degree relatives with invasive breast cancer (see above).

Note: Telehealth services are available for women living in remote areas.

**PRACTICE POINT**

*Transmission of hereditary breast cancer can be through either **maternal** or **paternal** lineage*

## Evidence-based Implementation Considerations

In Alberta between January 2010 and December 2011, 45.2 % of women aged 50 to 69 did not receive a screening mammogram.[1] Screening participation rates are lower in Aboriginal women[2,3], new immigrants and women with low incomes.[4] The strongest stimulus for a woman to participate in mammography screening is the recommendation from a health care provider.

Discuss screening mammography with women of the appropriate age. Initiate opportunistic discussion when the woman presents for other health concerns. Outreach and preventive health screening checklists also increase the likelihood of engaging women to make informed decisions about breast cancer screening.

**PRACTICE POINTS**

*Initiate discussion about screening mammography with women of the appropriate age*

*Use outreach, opportunistic screening and checklists to increase the likelihood of engaging women to make informed decisions about screening*

# Background

## Risk

Breast cancer is the most common form of cancer in women in Alberta other than non-melanoma skin cancer.[5] Approximately 1 in 8 women is expected to develop breast cancer during her lifetime, and 1 in 31 will die from the disease.[6] Age and heredity are major non-modifiable risk factors. Breast density, certain benign breast conditions, several reproductive factors, and a history of chest wall radiation also increase a woman's risk. Modifiable lifestyle factors such as body weight, physical activity, alcohol consumption, and smoking should be addressed in the context of an overall wellness strategy.

## AGE

As women get older their risk of breast cancer increases (see Table 1).

| Age Group | Probability of Developing Breast Cancer, Females, 2006 - 2010 | Probability of Dying from Breast Cancer, Females, 2006 - 2010 |
|---|---|---|
| Lifetime Risk (all ages) | 1 in 8 | 1 in 31 |
| 0-20 | Less than 1 in 10,000 | Less than 1 in 10,000 |
| 20-30 | 1 in 1,695 | Less than 1 in 10,000 |
| 30-40 | 1 in 245 | 1 in 2,303 |
| 40-50 | 1 in 71 | 1 in 653 |
| 50-60 | 1 in 43 | 1 in 291 |
| 60-70 | 1 in 29 | 1 in 173 |
| 70-80 | 1 in 27 | 1 in 112 |
| 80+ | 1 in 24 | 1 in 51 |

*Table 1: Probably of Developing and Dying from Breast Cancer by Age, Females, Alberta, 2006 – 2010. Reproduced with permission from: Cancer Surveillance, Alberta Health Services, 2012.*[6]

The most recent report on breast cancer statistics in Alberta indicates that from 1990 to 2010 female breast cancer incidence rates remained stable and mortality rates decreased.[6] Mortality rates for women less than 50 years decreased by an average annual rate of 3.9%. The corresponding decreases in mortality rates for the 50 to 69 and the 70+ age groups were 2.9% and 1.7% annually respectively.[6]

## HEREDITY

Family History: Having one or two affected first degree relatives is associated with a lifetime excess incidence of breast cancer of 5.5% and 13.3% respectively.[7] The increase in risk is greater for younger women and is greater when the relative was affected at a younger age.[7]

Known Mutations: The prevalence of BRCA1 and BRCA2 mutations in the general population has not been well established; however, modeling estimates are between 1 in 300 and 1 in 500 depending on the ethnicity of the population.[8] Approximately 1 to 2% of all women with breast cancer will have a BRCA1 or BRCA2 mutation.[9] The meta-analytic mean cumulative risks for breast cancer at age 70 for women carrying BRCA1 or BRCA2 mutations are 57% (95% CI: 47-66%) and 49% (95% CI: 40-57%) respectively.[10] Men and women can pass on these hereditary cancer risks to their children and transmission is autosomal dominant so each child has a 50/50 chance of inheriting these gene mutations. It is important to assess history of cancer on both sides of the family.

The prevalence of BRCA mutation in the Ashkenazi Jewish population is as high as 1 in 40.[11] The family history threshold for referral to Medical Genetics is correspondingly lower for women with Ashkenazi Jewish ethnic heritage.

Breast cancer and ovarian cancer may occur in other genetic syndromes. Assessment, counselling and potential genetic testing for these syndromes will be considered by Medical Genetics Clinics.

Much of hereditary breast cancer and hereditary breast ovarian cancer is associated with mutations in genes that are currently unknown and for which testing is not available.

Refer to *Alberta Health Services, Risk Reduction and Surveillance Strategies for Individuals at High Genetic Risk for Breast and Ovarian Cancer (2011)*, available at: http://www.albertahealthservices.ca/1749.asp

## Biopsy Proven Atypical Hyperplasia or Lobular Carcinoma In Situ

In women with a history of breast biopsies showing atypical hyperplasia or lobular carcinoma in situ the risk of breast cancer is increased by at least four-fold and the increased risk persists for at least 25 years.[12]

## Chest Wall Radiation

Women with a history of chest wall radiation as treatment for another cancer have up to a ten-fold increased risk for breast cancer. The risk varies according to the patient's age when she had radiation therapy and is highest if the radiation was given before menarche.[13]

## Breast Density

There is an inverse relationship between breast density and age; younger women are more likely to have dense breast tissue than older women (see Figure 1). Although breast density generally decreases with age, there are outliers at both ends of the age spectrum with some young women having fatty breasts and some older women having extremely dense breasts.[14] Women with extremely dense breasts have about a two-fold increased risk compared to women with breasts of average density.[15]

Breast density is a mammographic finding and cannot be reliably defined by a physical exam. Dense breast tissue is known to limit the sensitivity of mammographic screening.[14] In one study, the sensitivity of screening mammography was 72% overall, but it declined sharply from 80% to 59% to 30% for women with predominantly fatty breasts, heterogeneously dense breasts, and extremely dense breasts respectively with a commensurate increase in interval cancer rate.[16] Although the assessment of breast density is not reliably reproducible, the reporting of radiological breast density provides a general idea of the likelihood that cancer will be detected or missed. When a radiological assessment determines that breast density is high, annual mammography may be suggested by the radiologist. There is inadequate outcome data upon which to base a separate screening guideline that would apply routinely for women with dense breasts.

Once diagnosed with breast cancer, women with high density breasts do not have a higher risk of death from breast cancer than women with lower density breasts after controlling for stage.[17]

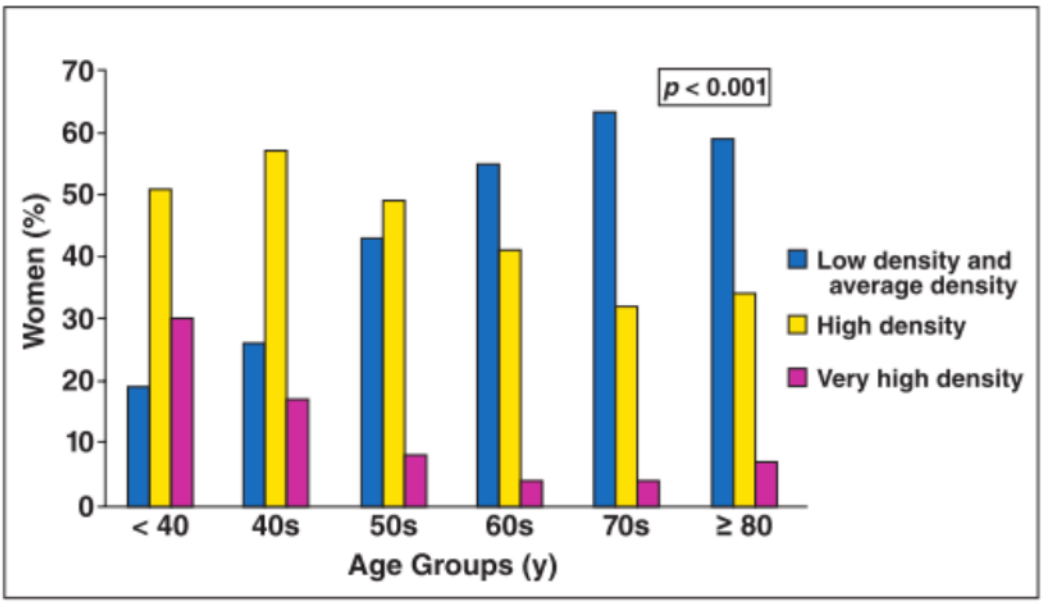


*Figure 1: Bar graph shows patient age and categories of breast density. Reproduced with permission from: American Journal of Roentgenology.*[14]

## HORMONAL INFLUENCES

Menarche and Menopause: Women with earlier age of menarche[18] and/or later age of menopause[19] have an increased risk of breast cancer, mediated in part by the increased number of menstrual cycles and the longer lifetime exposure to estrogen and progesterone.

Reproductive History: Nulliparity also increases a woman's risk of breast cancer and every live birth reduces the relative risk by about 7%.[18] Women 30 years or older at the time of their first live birth have a higher risk of breast cancer than women having their first child at a younger age.[18] The risk is about 20% higher than for women whose first birth was at age 25 to 29, but is about 25% lower than nulliparous women. Evidence from well conducted prospective studies indicate that neither spontaneous nor induced abortion increases a woman's breast cancer risk.[20]

Breastfeeding: Reduced lifetime exposure to estrogen and progesterone may also explain the protective effect conferred by increasing duration of breastfeeding. The relative risk of breast cancer decreases by about 4% for every 12 months of breastfeeding.[21]

Hormone Replacement Therapy: Among women who use combination estrogen-progesterone hormone replacement therapy (HRT), the risk of breast cancer increases with the length of use.[22] After five years of using combined HRT, the risk of breast cancer increases by about 15%, and the risk returns to baseline within about two years of stopping HRT.[23] Estrogen therapy alone increases breast cancer risk as well, but the increased risk is lower than for combined therapy. [22,23]

## OBESITY

Obesity is associated with an increased risk of postmenopausal breast cancer, as is weight gain throughout adulthood.[24] Obesity also negatively affects prognosis of early stage breast cancer.[25]

### LIFESTYLE

Physical Activity: Breast cancer risk is reduced by about 25% among physically active women compared to the least active women.[26] The evidence is strongest for recreational activity, for activity of at least moderate intensity, and for activity sustained over a lifetime.[26]

Alcohol Consumption: Regular consumption of as little as one drink per day elevates the risk of breast cancer by about 4%.[27] The risk increases steadily with increasing consumption regardless of the type of alcohol consumed. Also, there may be a case for alcohol use being more strongly associated in risk of hormone-sensitive breast cancers.[27,28]

Smoking: The Canadian Expert Panel on Tobacco Smoke and Breast Cancer Risk suggests that the association between active smoking and breast cancer is consistent with causality.[29] Also, the association between second hand smoke and breast cancer among younger, primarily premenopausal women who have never smoked is consistent with causality.[29] Further research is required to determine the magnitude of the effect.

### NEGLIGIBLE RADIATION RISK

The risk of mammographically-induced cancer is generally considered to be negligible because of the very low doses of radiation and the relative insensitivity of the mature breast to ionizing radiation.[30,31,32] Studies that raised this concern involved much higher levels of radiation than are used today.

## SCREENING RECOMMENDATIONS

### MAMMOGRAPHY

Mammography is the recommended method of breast cancer screening for the average risk population. It is the only screening modality shown to reduce breast cancer mortality. Possible risks include false negative results and a false sense of security that may delay diagnosis; extra tests and anxiety associated with false positive results; and the fact that breast cancer may be diagnosed with no improvement in the length or quality of life.[33] Recommendations are provided in age categories; however there are no rigid delineations between these categories. Clinical judgment may be used to adjust the frequency of screening considering individual differences. As compared to the Toward Optimized Practice 2007 guideline, the age categories have been re-defined to: 50 to 74 years and 75 years and older, to reflect increasing life expectancy and associated screening needs.

39 Years and Under: For women 39 years and under, breast cancer screening is not recommended because the incidence of breast cancer is low in this age group[6] and there is no evidence for mortality reduction.[33]

40-49 Years: While mortality reductions have been demonstrated for the 40 to 49 year age group, the balance of benefits to risks is not strong enough to recommend routine screening. For women 40 to 49 years, the number needed to screen (NNS) to prevent one death is 2108.[33] In comparison to older women, the absolute benefit from screening in this age group is lower because the overall risk of cancer is lower[33]. With a lower prevalence, a higher proportion of positive results are false-positive

results requiring additional follow-up tests.[33] In determining whether to screen in this age group, health care providers are encouraged to engage women in a discussion about the benefits and risks of screening. Refer to http://www.phac-aspc.gc.ca/cd-mc/mammography-mammographie-eng.php

The ideal screening interval for this group is also less clear. Due to the higher prevalence of very high breast density, screening mammography is more likely to miss cancer in this age group.[14] It has also been suggested that more rapid growth of tumours and sojourn time (time from onset of cancer to the presence of symptoms) in younger women support a shorter interval between screenings.[34,35,36] Expert opinion, based on sojourn period, is that for women 40 to 49 choosing to be screened in Alberta the recommended interval is one year.

50-74 Years: The strongest evidence of mortality reduction associated with mammography screening is in the 50 to 69 year age group.[33] The benefit is greater for the upper half of this age group, i.e., the NNS to prevent one death is 910 for women 50 to 59 years and the NNS is 432 for women 60 to 69 years. Few breast cancer screening trials have included women 70 to 74. These few studies demonstrated mortality reductions at least as large as for women 50 to 69, but with inadequate power to reach statistical significance. Given the high incidence of breast cancer in the 70 to 74 year age group, the benefit of screening mammography is expected to be similar to 50 to 69 years.[33]

Routine screening every 2 years is recommended for women 50 to 74. While one trial in the United Kingdom showed no difference in mortality between women randomized to annual versus triennial screening, the tumours detected in the annual group were significantly smaller.[37] Modelling studies support a two year interval and suggest that compared to annual screening, biennial screening preserves 80% of the benefit with almost 50% fewer false positive results.[38]

75 Years and Older: There are no studies on the benefit of screening for women 75 years and older; however these women are at increased risk for developing breast cancer[5] and may benefit from screening. Health care providers should consider individual health factors and the woman's preference to continue screening. The recommended screening interval is every 2 years.

## *Clinical Breast Examination (CBE) and Breast Awareness*

No trial has ever examined whether the addition of CBE to screening mammography reduces mortality. Although some cancers may be identified by CBE[39], there is no evidence that CBE results in fewer deaths. CBE is not very specific and generates a significant number of false positive results.[40] Based on expert opinion, it is recommended that CBE is considered as part of the physical examination and a teaching opportunity to discuss breast health. Women should be familiar with their breasts and encouraged to report changes; in particular, nipple discharge, rash on nipples, inversion, dimpling or new mass in the breast or axilla.[41]

## *Other Technology*

Magnetic Resonance Imaging (MRI): To date, MRI screening studies have focused on high risk women, and there are limited studies evaluating the use of MRI for screening in the average risk population.[33] MRI may be used in specific circumstances as determined by a radiologist.

Ultrasound: There is insufficient evidence to support the use of ultrasound for routine screening in the average risk population. Ultrasound should not be used as a stand-alone screening test. It may

have a role as an adjunct to mammography in screening women with dense breasts, as determined by a radiologist. Ultrasound helps to detect small, mammographically occult cancers; however, the overall positive predictive value of screening ultrasound is low.[42]

Tomosynthesis: Tomosynthesis is a new 3D technology which may prove of diagnostic benefit in denser breasts. Further studies are required to establish the role of tomosynthesis in breast cancer screening. Tomosynthesis may be used in specific circumstances, as determined by a radiologist.

Thermography: There is no evidence that thermography reduces mortality related to breast cancer.[43,44] It may lead to a false sense of security and potential harm. Women should be discouraged from using thermography for the detection of breast cancer.

### *HIGH RISK POPULATION*

The recommendations for the high risk population were developed in response to feedback from family physicians requesting guidance for those women requiring more intensive screening than those of average risk and also those women requiring referral to medical genetics.

Recommendations are based on best evidence and program considerations developed by an expert panel from the high risk clinics and medical genetic clinics in northern and southern Alberta and are consistent with other medical genetic clinics in Candada.

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## *SUGGESTED CITATION*

Toward Optimized Practice (TOP) Working Group for Breast Cancer Screening. 2013 Sep. Breast cancer screening: clinical practice guideline. Edmonton, AB: Toward Optimized Practice. Available from: http://www.topalbertadoctors.org

For more information see www.topalbertadoctors.org

Early Detection of Breast Cancer – April 1999
Reviewed – August 2000
Reviewed – March 2002
Reviewed – November 2004
Revised – March 2009
Revised – September 2013
Minor revision July 2015

# APPENDIX A

## GENERAL RESOURCES

- Information on Mammography for Women Aged 40 and Older: A Decision Aid for Breast Cancer Screening in Canada, Public Health Agency of Canada, 2009. Available at: http://www.phac-aspc.gc.ca/cd-mc/mammography-mammographie-eng.php
- Breast Cancer Screening. Information available at: www.ScreeningforLife.ca/breastcancer

## RESOURCES FOR HIGH RISK POPULATION

- Calgary Cancer Genetics Clinic: Dr. R.B. Lowry Genetics Clinic, Alberta Children's Hospital, 2888 Shaganappi Trail NW, Calgary, AB T3B 6A8. Phone: (403) 955-7137, Fax: (403) 955-2701.
- Calgary High Risk Breast Cancer Clinic: The High Risk Breast Cancer Clinic, Calgary Zone Alberta Health Services accepts referrals using the Central Access and Triage system. Phone (403) 944-2240.
- Edmonton Cancer Genetics Clinic Referral Criteria: www.medicalgenetics.med.ualberta.ca. Edmonton Medical Genetics Clinic, 8-53 Medical Sciences Building, University of Alberta, Edmonton, Alberta T6G 2H, Phone: (780) 407-7333, Fax: (780) 407-6845.
- Allard Hereditary Breast and Ovarian Clinic, Royal Alexandra Hospital, Robbins Pavilion, Ground Level, 10240 Kingsway Avenue, Edmonton, Alberta, T5H 3V9, Phone: (780) 735-4718, Fax: (780) 735-4020.
- Alberta Health Services. Risk Reduction and Surveillance Strategies for Individuals at High Genetic Risk for Breast and Ovarian Cancer (2011), available at: http://www.albertahealthservices.ca/1749.asp