Alberta Breast Cancer Screening

Clinical Practice Guideline 2022 Update

GOAL

To provide updated evidence-based guidance on screening for breast cancer. To help Albertans and their healthcare providers make informed choices about breast cancer screening.

TARGET POPULATION

Asymptomatic women, transgender, gender diverse, and non-binary people* of all ages

Exclusions

- Persons with signs and symptoms suggesting breast cancer
- Persons currently being treated for breast cancer
- Cisgender† men

These guidelines have not been updated since the last full update was completed in 2013. Since that time, new evidence has become available and other new guidelines have been published. The updated Alberta Breast Cancer Screening Clinical Practice Guidelines include new recommendations based on this new information.

Methodology for Guideline Review

A provincial breast cancer screening clinical practice guideline committee was funded by the Alberta Medical Association's Accelerating Change Transformation Team (ACTT) for guideline review and update. The committee has representation from radiology, family medicine, nursing, medical oncology, public health & preventative medicine, surgery and the public. The topics of special interest (e.g. breast density, higher-than-average risk, tomosynthesis, recommended screening ages, etc.) were reviewed using systematic reviews, expert opinion, Alberta breast cancer screening data and micro-simulation modeling. Following evidence synthesis, committee members developed recommendations through careful consideration of the benefits and harms as well as the strength of the current evidence. A modified Delphi process was used to reach consensus and determine the best option. The guidelines herein represent the collective input of the experts on the committee. As new information becomes available, the balance of benefits and harms may change. As such, recommendations will continue to be updated accordingly.

*Transgender, gender diverse and non-binary people refers to those who are:
1) Assigned female at birth and have not undergone top surgery (mastectomy); or
2) Assigned male at birth and have been on feminizing hormone therapy for 5 or more years in total.

†Cisgender refers to people who have a gender identity that matches the sex they were assigned at birth.

Summary of Clinical Practice Guideline 2022

EVIDENCE | PATIENT RESOURCES | HCP RESOURCES | SCREENING FORLIFE.CA

Average-Risk Population: Recommendations →

Individuals who do not meet any of the criteria for higher-than-average risk or high risk are considered average risk. The majority of people fall into the average-risk category.

USE DIGITAL MAMMOGRAPHY (DM) FOR SCREENING →

39 YEARS & UNDER	40 TO 44 YEARS	45 TO 74 YEARS	75+ YEARS*
Screening is **not** recommended	Routine screening is **not** recommended. It may be considered based on informed discussion and individual preference.	Screening recommended	Consider individual health factors and personal preference to continue screening
	For those individuals requesting screening, the optimal interval is one year	Screen every 2 years	

Persons with surgery for breast augmentation, breast reduction, as well as transgender, gender diverse and non-binary (as defined on page 1): Follow above recommendations for mammographic screening in the average-risk population. Mention presence of implants in history section of mammography requisition.

OTHER SCREENING-RELATED TECHNOLOGY →

Digital Breast Tomosynthesis (DBT/3D mammography): 2D digital mammography remains the standard for screening average-risk individuals. At the present time there is not enough evidence to provide a strong recommendation for or against the use of DBT (3D mammography) in the average-risk population.

Ultrasound: Not recommended as a standalone screening test for the average-risk population. May be used as a supplemental tool by a radiologist after considering current and prior imaging (if available), and history.

Magnetic Resonance Imaging (including fast/abbreviated MRI): Not recommended as a screening test for the average-risk population.

Thermography: Do not use thermography as a screening test for breast cancer. There is no evidence to support thermography for breast cancer screening or as an adjunct to mammography. Breast thermography is not approved by Health Canada for use in breast cancer screening.

Key Discussion Points for Healthcare Providers and their Patients

1. Perform an assessment of breast cancer risk →

An assessment for breast cancer risk should occur for all individuals. It should be opportunistic and periodic. Consider a person's age, medical history, maternal and paternal family history, mammographic density and other associated risk factors in determining their screening recommendations (see next page).

2. Initiate discussion about breast cancer screening with individuals of the appropriate age, including potential benefits and risks →

To reduce anxiety, healthcare providers should remind individuals of the possibility of additional tests needed beyond the initial screening modality. For age-specific benefits and risks, refer to *"Making an Informed Decision About Breast Cancer Screening."* Available at: screeningforlife.ca/for-health-providers

3. Encourage breast awareness →

Individuals should report changes in their breasts, with particular attention to: nipple discharge/rash/inversion, skin dimpling, or new mass in the breast or axilla.

4. Discuss modifiable risk factor(s) →

While some risk factors for breast cancer are not modifiable (e.g., gene mutation, breast density), the ones more amenable to modification include: alcohol consumption, inactivity, obesity and smoking. These should be addressed in the context of overall disease prevention, as should appropriate use of hormone replacement therapy.

*The decision to continue screening is an individual one that should be made in conjunction with one's healthcare provider. If life expectancy is less than 10 years based on other comorbidities, individuals are unlikely to experience meaningful benefit from continued screening.

Updated: Jan 2022

Summary of Clinical Practice Guideline 2022

REFERRAL CRITERIA | BREAST DENSITY | RISK FACTORS | SCREENING FORLIFE.CA

Higher-than-Average Risk Population: Recommendations

Individuals requiring more intensive screening →

RISK FACTOR	RECOMMENDATION*
Breast density **(category D – extremely dense) and** age 45+	▪ Annual mammography AND ▪ Consider annual breast ultrasound ▪ Consider annual clinical breast exam
Breast biopsy showing certain benign breast conditions known to increase risk (atypical hyperplasia or lobular carcinoma in situ)	▪ Annual mammography ▪ Consider annual clinical breast exam
Previous history of ductal carcinoma in situ +/- invasive breast cancer	▪ Annual mammography ▪ Consider annual clinical breast exam
Family history of breast cancer in a first-degree relative but not meeting criteria for Medical Genetics or the Hereditary Breast and Ovarian Cancer (HBOC) Clinic	▪ Annual mammography starting 5 to 10 years younger than the youngest case in the family, but no earlier than age 30 and no later than age 40 ▪ Consider annual clinical breast exam

High Risk Population: Recommendations →

Individuals requiring referral to a high risk clinic/genetics for screening recommendations

RISK FACTOR	RECOMMENDATION*
History of chest wall radiation (i.e., radiation for treatment for Hodgkin Lymphoma) at age 30 or younger	Starting at 5-10 years following radiation, but no earlier than age 30 and no later than age 40: ▪ Annual clinical breast exam ▪ Annual mammography ▪ Annual screening breast MRI until age 70
High risk due to family history +/- germline mutation as assessed by Medical Genetics or HBOC Clinic	Follow screening and risk reduction recommendations as per Medical Genetics or HBOC Clinic (see appendix A)

CLINICAL BREAST EXAM (CBE) →

- There is no evidence that routine CBE reduces breast cancer mortality. It should not replace mammography for screening.
- However, CBE is encouraged as part of a periodic physical exam, as it provides an opportunity to discuss breast awareness with the patient (see below).
- CBE should be included in the work up for any new breast symptom.

Breast Awareness: Breast awareness is the practice of becoming familiar with the look and feel of one's own breasts over time. Specific changes to be aware of include—but are not limited to - new lumps, nipple inversion/discharge/crusting/bleeding/rash, dimpling or thickening of the skin in one area of the breast. Any changes or concerns should be discussed promptly with a healthcare provider.

Breast Self-Examination (BSE): BSE is the practice of regularly checking one's own breasts for signs of breast cancer. Evidence has shown that the harms of this **practice outweigh the benefits for the average-risk population. Therefore, BSE is not recommended as a cancer screening method for the average-risk population.**

*The decision to continue screening is an individual one that should be made in conjunction with one's healthcare provider. If life expectancy is less than 10 years based on other comorbidities, individuals are unlikely to experience meaningful benefit from continued screening.

Updated: Jan 2022

Evidence-based Implementation Considerations

In Alberta between January 2018 and December 2019, 35.1% of eligible Albertans aged 50 to 74 did not receive a screening mammogram.[1] Screening participation rates are lower in Indigenous people,[2,3] new immigrants, and people with low incomes.[4] Recommendations to screen from a healthcare provider have the biggest impact on whether or not a person participates in mammography screening.[5]

- Perform a risk assessment to stratify an individual's breast cancer risk (i.e. average, higher-than-average, or high-risk).
- Discuss breast cancer screening with individuals of appropriate age. Use shared decision making as part of this conversation to make the decision based on the individual's relative value that they place on the benefits and risks of screening.
- If deciding to screen, review the importance of continued regular screening and review follow up screening interval recommendations after each screen.
- Capitalize on the opportunity to discuss breast cancer screening not just at periodic health visits, but also opportunistically when individuals present for other health concerns.
- Make use of outreach, preventive health screening checklists, and electronic medical records reminders to increase the likelihood of individuals staying up to date with breast cancer screening.

Background

RISK FACTORS

Breast cancer is the most common form of cancer in women in Alberta, apart from non-melanoma skin cancer.[6] Approximately 1 in 7 women are expected to be diagnosed with breast cancer during their lifetime, and 1 in 35 will die from the disease.[7] Age and family history are major non-modifiable risk factors. Other non-modifiable risk factors include breast density, certain benign breast conditions (atypical hyperplasia, lobular carcinoma in situ, etc.), several reproductive factors, and a history of chest wall radiation. Modifiable lifestyle factors such as body weight, physical activity, alcohol consumption, and smoking should be addressed in the context of overall wellness and breast cancer risk reduction.

ABSOLUTE VS RELATIVE RISK

When looking at the impact a risk factor has on breast cancer risk, it is important to remember the difference between absolute risk and relative risk.

Absolute Risk: Looks at the total risk of developing a disease.

For example, if your odds of developing breast cancer are 1 in 7, the risk is about 14%. If a certain risk factor changes the odds to 1 in 6, about 17%, the difference would be 17% - 14% = 3%. This means the absolute risk has increased by about 3%.

Relative Risk: Looks at the change in risk as a proportion of the total risk. This can make the impact of a change appear much more significant.[8]

Using the previous example, the change in relative risk would be 3% ÷ 14% = 21%. This means the relative risk has increased by about 21%.

Note: To avoid repetition, the type of risk used in this guideline is always relative risk, unless otherwise specified. This is due to the fact that relative risk is generally what is cited in the literature.

Non-modifiable Risk Factors

1. AGE

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

AGE GROUP	PROBABILITY OF DEVELOPING BREAST CANCER, FEMALES, 2014 - 2018	PROBABILITY OF DYING FROM BREAST CANCER, FEMALES, 2014 - 2018
Lifetime Risk (all ages)	1 in 7	1 in 35
0-20	Less than 1 in 10,000	Less than 1 in 10,000
20-30	1 in 1,364	Less than 1 in 10,000
30-40	1 in 226	1 in 2,859
40-50	1 in 69	1 in 802
50-60	1 in 43	1 in 344
60-70	1 in 28	1 in 202
70-80	1 in 24	1 in 124
80+	1 in 7	1 in 55

Table 1: Probably of Developing and Dying from Breast Cancer by Age, Females, Alberta, 2014–2018. Reproduced with permission from: Cancer Surveillance, Alberta Health Services.[8]

2. FAMILY HISTORY

Family History: It is important to assess history of cancer on both sides of the family. Having one or two first degree relatives affected by breast cancer is associated with a lifetime increased incidence of breast cancer of 5.5% and 13.3%, respectively.[10] The increase in relative risk is greater for younger individuals and is greater when the affected relative was diagnosed at a younger age.[10]

Known Mutations: BRCA mutations are alterations to genes (mainly BRCA1 and BRCA2 genes) that normally help protect against breast cancer. Mutations to these genes can increase the risk of developing breast cancer. The cumulative lifetime risk of breast cancer is estimated to be 72% for BRCA1 and 69% for BRCA2 carriers, up to the age of 80.[11] The prevalence of BRCA1 and BRCA2 mutations in the general population has not been well established; however, modeling estimates are between 1 in 300 (0.3%) and 1 in 500 (0.2%) depending on ethnicity*.[12] However, approximately only 1 to 2% of breast cancer cases have a BRCA1 or BRCA2 mutation.[13] Both men and women can pass on these gene mutations to their children; 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.

Aside from BRCA mutations, other genetic syndromes may increase the risk of breast cancer and ovarian cancer. Clinics will consider assessment, counselling, and potential genetic testing for these syndromes, as appropriate. However, there may also be some mutations that increase risk of breast cancer, but whose exact identification is currently unknown and for which genetic testing is not available.

Medical Genetics referral should be made for a patient when they have a personal and/or family history as outlined in Appendix A.

3. BREAST DENSITY

Below is a brief overview of breast density. For more information, including printable resources for both patients and healthcare providers, visit screeningforlife.ca/for-health-providers and select either Patient Education Resources (for patients) or Shared Decision Making (for healthcare providers).

Breast density refers to the amount of dense tissue compared to non-dense (fatty) tissue in the breasts. There are four categories of breast density (American College of Radiology categories A-D):

A The breasts are almost entirely fatty.

B There are scattered areas of fibroglandular density.

C The breasts are heterogeneously dense, which may obscure small masses.

D The breasts are extremely dense, which lowers the sensitivity of mammography.

There is an inverse relationship between breast density and age—younger people are more likely to have dense breast tissue (category C or D) compared to older people (see Figure 1). Although breast density generally decreases with age, there are outliers at both ends of the age spectrum—some younger individuals have fatty breasts, while some older individuals have extremely dense breasts.[14] For people with extremely dense breasts, the relative risk of developing breast cancer is about 2.1 times greater than average.[15] However, it should be noted that age remains a greater determinant of breast cancer risk than breast density alone.

*In the Ashkenazi Jewish population it can be as high as 1 in 40 (2.5%)[16]

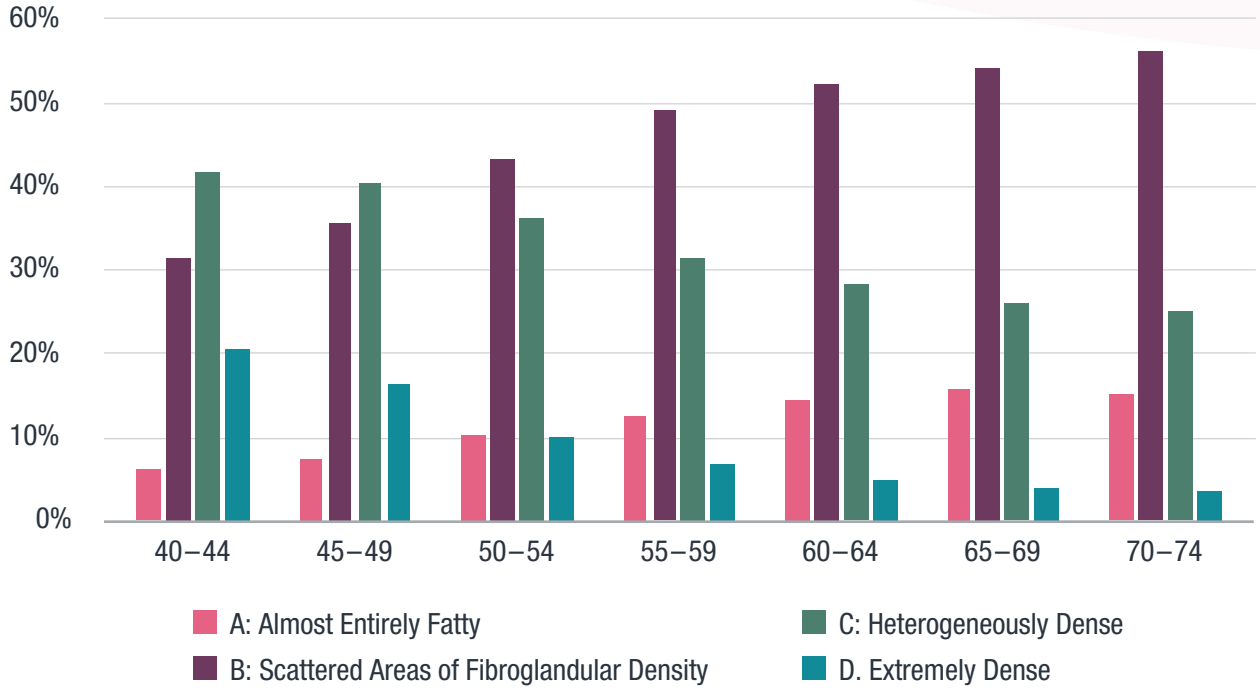

Figure 1: Bar graph shows patient age and categories of breast density in Alberta for 2019.[16]

Breast density is a mammographic finding which cannot be reliably defined by a physical exam. Dense breast tissue limits the sensitivity of mammographic screening.[14] In one study, the sensitivity of screening mammography was 72% overall, but declined sharply from 80% to 59% to 30% for people with predominantly fatty breasts, heterogeneously dense breasts, and extremely dense breasts, respectively—with a commensurate increase in interval cancer rate.[17] Breast density may be assessed by the radiologist or by software designed to score breast density. The reporting of radiological breast density provides a general idea of the likelihood that cancer will be detected or missed.

Once diagnosed with breast cancer, people with high density breasts (category C or D) do not have a higher risk of death from breast cancer than people with lower density breasts after controlling for stage.[18]

4. HISTORY OF CERTAIN BENIGN BREAST CONDITIONS: BIOPSY-PROVEN ATYPICAL HYPERPLASIA OR LOBULAR CARCINOMA IN SITU

These are benign breast conditions but can elevate a person's risk to higher-than-average risk and require more intensive screening. In people with a history of breast biopsies showing atypical hyperplasia or lobular carcinoma in situ, the relative risk of breast cancer is increased by at least four-fold and the increased risk persists for at least 25 years.[19]

Visit the American Cancer Society to see a list of other non-cancerous breast conditions that **may or may not** increase an individual's risk of breast cancer.

5. HORMONAL INFLUENCES

Menarche and Menopause: Individuals with earlier age of menarche[20] and/or later age of menopause[21] have an increased risk of breast cancer, mediated in part by the increased number of menstrual cycles and longer lifetime exposure to estrogen and progesterone.

Reproductive History: Number of and age of delivery of successful pregnancies also affect a person's risk of breast cancer by way of affecting the number of lifetime menstrual cycles and cumulative estrogen/progesterone exposure. Every live birth reduces the risk of breast cancer by about 7%; additionally, the younger a person is at their first delivery, the lower their risk of breast cancer.[20]

Breastfeeding: Reduced lifetime exposure to estrogen and progesterone may also explain the protective effect conferred by increasing duration of breastfeeding. The risk of breast cancer decreases by about 4% for every 12 months of breastfeeding.[22]

Hormone Replacement Therapy (HRT): Among people who use combination estrogen-progesterone hormone replacement therapy, the risk of breast cancer increases with the length of use.[23] After five years of using combined HRT, the relative risk of breast cancer increases by about 15%, and the risk returns to baseline within about two years of stopping HRT.[24] Estrogen therapy alone increases breast cancer risk as well, but less so than for combined estrogen-progesterone therapy.[23,24]

6. CHEST WALL RADIATION

Individuals with a history of chest wall radiation as treatment for another cancer (such as Hodgkin lymphoma) have up to a ten-fold increased risk for breast cancer. The risk varies according to the patient's age at which they underwent radiation therapy—it is highest if the radiation was given before menarche.[25] Risk also varies with the dose of radiation administered.[26]

Modifiable Risk Factors

1. OBESITY

Obesity is associated with an increased risk of postmenopausal breast cancer, as is weight gain throughout adulthood.[27] Obesity also negatively affects the prognosis of early stage breast cancer.[28]

2. LIFESTYLE

In Alberta, approximately 26% of breast cancers are linked to modifiable risk factors.[29]
This equates to 620 cases that could be prevented every year.

A. Physical Activity: The relative risk of breast cancer is reduced by about 25% when comparing physically active people to the least active people.[30] The evidence is strongest for recreational activity, for activity of at least moderate intensity, and for activity sustained over a lifetime.[30]

B. Alcohol Consumption: Regular consumption of as little as one drink per day elevates the relative risk of breast cancer by about 4%.[31] Risk increases steadily with increasing consumption regardless of the type of alcohol consumed. There may also be a case for alcohol use being more strongly associated in risk of hormone-sensitive breast cancers.[31,32]

C. 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.[33] Also, the association between second hand smoke and breast cancer among younger, primarily premenopausal people who have never smoked is consistent with causality.[33] Further research is required to determine the magnitude of the effect.

D. Nutrition: Getting lots of fruits and vegetables into one's diet can also lower the risk of most cancers, including breast cancer. See Canada's Food Guide for more information on healthy eating.

Many of the modifiable risk factors for breast cancer are the same as for other types of cancer. A study by the Canadian Cancer Society identified the most beneficial behavioural changes to reduce one's chance of developing cancer (Figure 2). Modifiable risk factors for breast cancer specifically are presented in Figure 3. For information on modifiable risk factors for cancer, visit healthiertogether.ca.

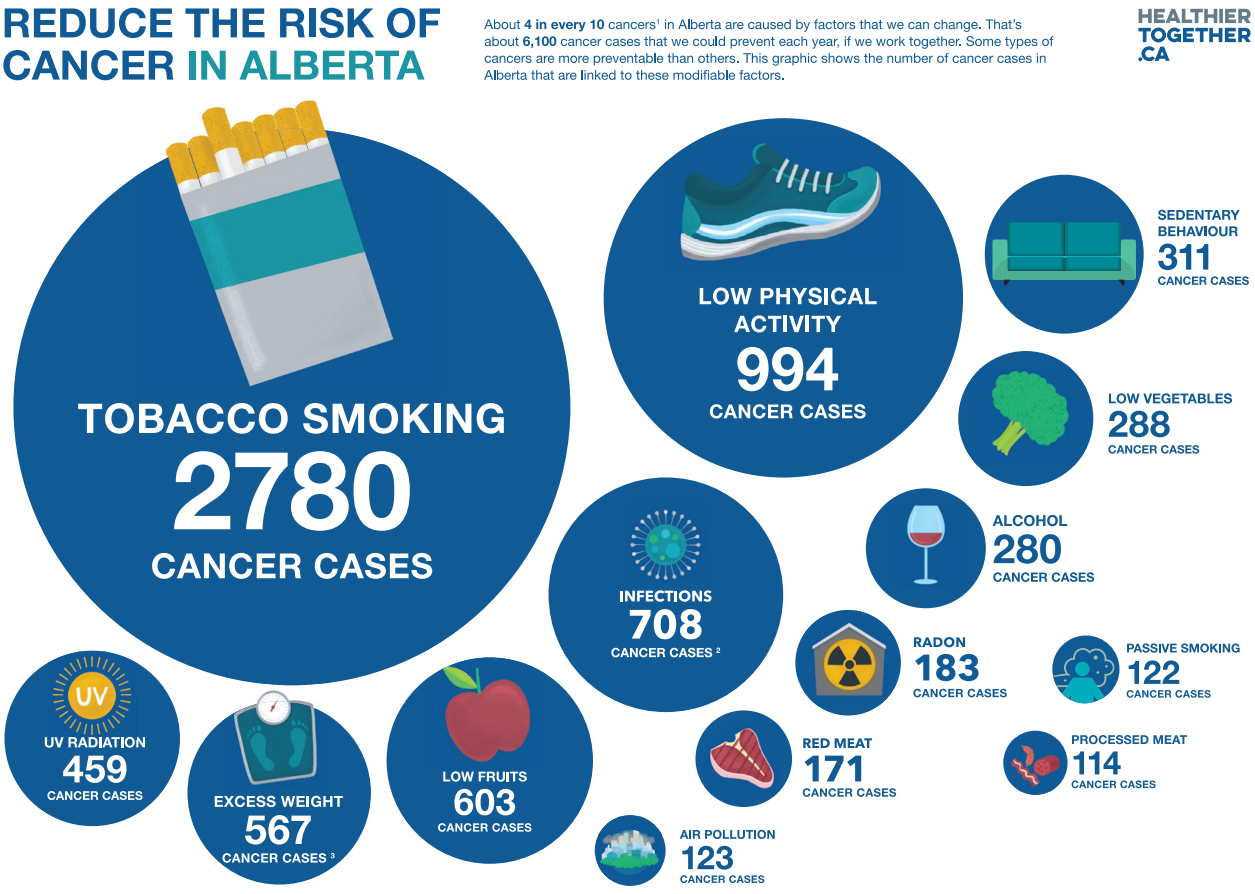

Figure 2: Preventable cancer cases in Alberta by modifiable risk factor. Alberta Risk Factor Infographic © 2020. Reproduced with permission from the Alberta Cancer Prevention Legacy Fund, AHS.[29]

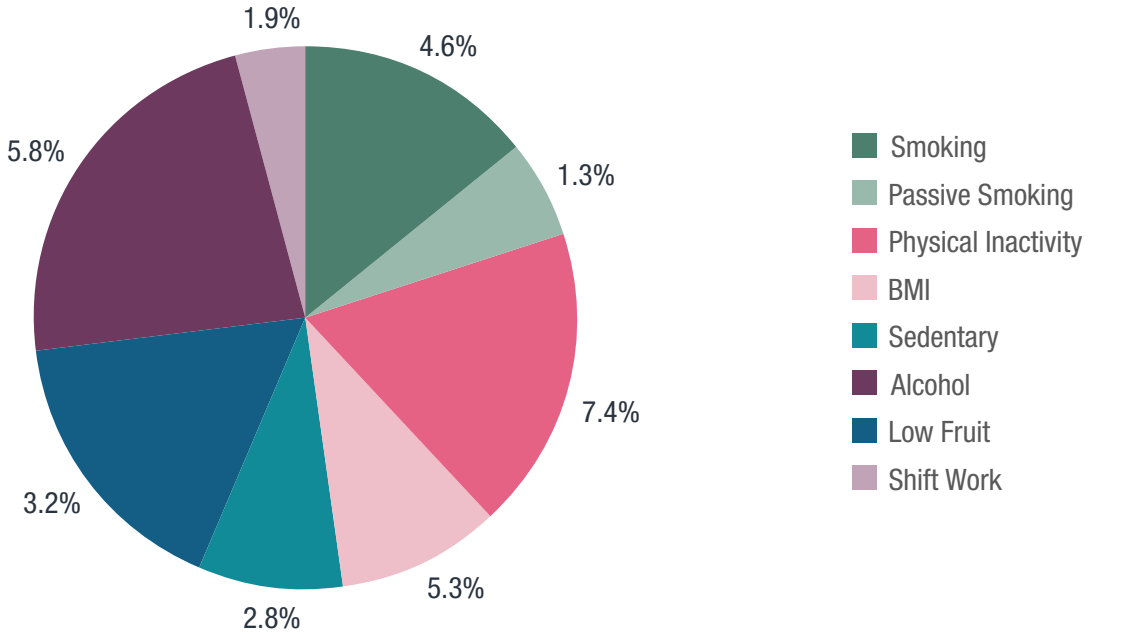

Figure 3: Population attributable risk for developing breast cancer in Canada. Alberta Risk Factor Infographic © 2020. Definitions are provided in Appendix C. Reproduced and modified with permission from the Alberta Cancer Prevention Legacy Fund, AHS.

Updates to Screening Recommendations

RISK ASSESSMENT

Screening for breast cancer should begin with an assessment of risk. Certain factors are known to increase breast cancer risk; these elevate a person's risk category from average-risk to higher-than-average risk and high risk. A discussion should occur about the benefits and risks of added screening modalities (screeningforlife.ca/for-health-providers—click on *"Shared decision making"* for healthcare provider resources, or *"Patient education resources"* for resources for patients).[34] A risk assessment tool (see the list of available risk assessment tools and what they measure at screeningforlife.ca) also provides additional insight about an individual's personal risk, but should not be solely relied on for clinical decision-making. In general, risk assessment tools have been found to have only moderate accuracy when applied to the general population.[35-37] At this time, it is not possible to recommend one tool over another.

Average-Risk Screening

Practice Point

The majority (80%+) of breast cancers occurs in people of average-risk.

DIGITAL MAMMOGRAPHY

Mammography is the recommended method of breast cancer screening for the average-risk population. Screening regularly with mammography has been shown to reduce breast cancer mortality by 30% to 40%—no other screening modality affects breast cancer mortality risk.[38] As with all screening programs, there are limitations patients and physicians should be aware of, including:

- **Overdiagnosis/overtreatment:** Cancer may be correctly diagnosed, but would not have become symptomatic in one's lifetime or affect one's life expectancy.[39] Treatment of these indolent (slow growing) cancers will continue to be an issue until available technology is good enough to differentiate these cases.
- **False positives:** Abnormal mammogram reported when cancer is not present, which leads to extra tests. In Alberta, approximately 94% of abnormal results do not result in a diagnosis of breast cancer.
- **Anxiety:** Concerns associated with false positive results.
- **False negative results:** Normal mammogram reported when cancer is actually present:
  - Lobular cancer and lobular carcinoma in situ are difficult to diagnose on mammography alone. This is an uncommon form of breast cancer and requires additional imaging (usually MRI) to make a diagnosis. *Clinicians and patients should be aware that a breast mass that is not seen on a mammogram may need additional work up for diagnosis*.
  - Breast density can also make breast cancer more difficult to detect.
- **False sense of security that may delay diagnosis:** Individuals do not report new breast concerns, since they believe they are safe from cancer after having a negative screen. This can be reduced through patient education.

A note about radiation risk from mammograms

Mammograms use very low doses of radiation. A screening digital mammogram is the equivalent to about 26 days of background radiation exposure from daily living, while DBT is equivalent to about 33 days.[40] Given the relative insensitivity of the mature breast to ionizing radiation, the risk of DM-induced cancer is generally considered to be very low.[41-43]

The standard for breast cancer screening remains 2D DM (with or without DBT). If using DBT, it should always be combined with either 2D synthetic (reconstructed two-dimensional images from DBT) or 2D DM for breast cancer screening. When using DBT in conjunction with DM the radiation

dose is approximately double that of DM alone.[44-46] However, it is still well within the limits set by the Canadian Association of Radiologists.

In summary, the amount of radiation exposure from DM alone or DM+DBT is so low that it should not be a deterrent to screening.[47] It is far more likely that a person's life will be saved by a screening mammogram (with or without DBT) than the risk of developing a radiation induced breast cancer.

RECOMMENDATIONS BY AGE

Breast cancer incidence increases with age (Figure 4). Recommendations are therefore provided in age categories; however, there are no rigid delineations between categories. Clinical judgment should be used to adjust the frequency of screening, when considering individual differences.

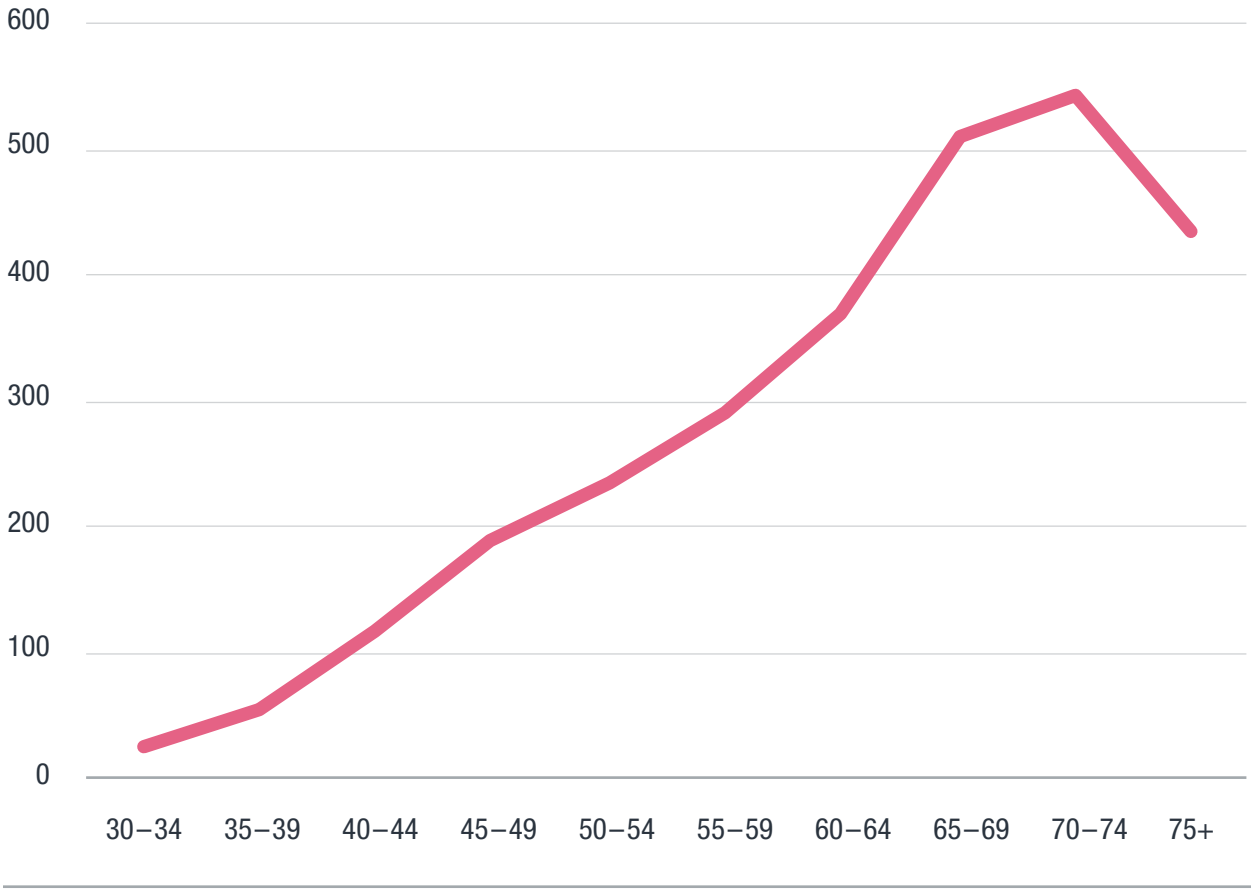

Figure 4: Alberta breast cancer (all types) iincidence per 100,000 in 2018 by age.

39 Years and Under: For individuals 39 years and under, breast cancer screening is not recommended.

As the risk of breast cancer increases with age, the incidence of breast cancer is very low in this age group[7] and there is no evidence for mortality reduction from screening in this group.[39] Additionally, the harms of breast cancer screening remain.

40-44 Years: Screening for ages 40-44 is **not** recommended.

The incidence of breast cancer is low in this age group.[9] While small mortality reductions have been demonstrated for this age group, the balance of benefits to harms is not strong enough to recommend routine screening. In comparison to older people, the absolute risk reduction from screening in this group is smaller because the overall risk of cancer is lower.[39] With a lower overall incidence of cancer, a higher proportion of positive results are false-positives and thus necessitate additional follow-up tests.[39] This can lead to unnecessary anxiety, procedures, increased radiation exposure, and potential discouragement of the patient from further breast cancer screening. Additionally, younger individuals can experience faster-growing and more aggressive cancer than older individuals.[49-52] This makes it less likely that breast cancer screening will detect a cancer before it becomes symptomatic.

The ideal screening interval for this age group is also less clear than for other age groups. Due to the higher prevalence of high breast density (increased breast density has a masking effect on mammography abnormalities), screening mammography is also more likely to miss cancer in this age group.[14] It has also been suggested that more rapid growth of tumours and shorter sojourn time (time from onset of cancer to the presence of symptoms) in younger people support a shorter interval between screenings.[48-51] If choosing to screen, expert opinion recommends screening every year in Alberta. Screening in this age category should only be done on people who choose to screen after having an informed discussion with their healthcare provider about the less favourable balance of benefits and harms of screening.

UPDATED AGE GROUP

45-74 Years: Routine screening every 2 years is recommended for individuals 45 to 74.

The strongest evidence of mortality reduction associated with mammography screening is in the 50 to 69 year age subgroup.[39] The benefit is greater for the upper half of this age group, i.e., the number needed to screen (NNS) to prevent one death is 910 for those aged 50 to 59 years, while the NNS is 432 for those aged 60 to 69 years. Few breast cancer screening trials have included people aged 70 to 74; these studies demonstrated mortality reductions at least as large as for people aged 50 to 69. 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 that for the 50 to 69 year age group.[39]

The decision to lower the recommended screening age from 50 to 45 was based on multiple factors. Under the previous recommendations, participation rates for people in Alberta aged 45-49 were 24%.[52] By contrast, participation rates for the recommended screening age groups, 50-74, were 65%.[53] Despite the lower volume of screening in the 45-49 year-old age group when following previous guideline recommendations, 246 breast cancers were detected in Albertans aged 45-49 in 2018, compared with 287 breast cancers in Albertans aged 50-54.[54] New evidence reviews also demonstrated a mortality reduction by starting screening prior to age 50.[39,49,55,56] On the other hand, it should be noted that people in their 40s experience higher abnormal (recall) rates (12%) compared with people aged 50-74 (8%).[57,58] This can further lead to more invasive testing, such as biopsies.

Another consideration is the recommended screening interval. While one trial in the United Kingdom showed no difference in mortality between people randomized to annual screening versus triennial screening, the tumours detected in the annual group were significantly smaller.[59] Modelling studies

suggest that compared to annual screening, biennial screening preserves at least 80% of the benefit of annual screening with almost 50% fewer false-positive results.[60]

DATA-MODELING

Population-based screening programs are carefully designed to bring the benefits of early cancer detection to a large number of seemingly healthy individuals. However, screening tests can cause harms to individuals, mostly in the form of additional tests and anxiety due to false positives. Since screening additional people means the possibility of increased harms and increased costs to the healthcare system, the potential benefits must be carefully weighed against anticipated harms and cost-effectiveness.

An analysis comparing the benefits and harms of various breast cancer screening options in people aged 40-49 years in Alberta was conducted using OncoSim-Breast. OncoSim-Breast is a mathematical model that simulates the breast cancer natural history of the Canadian population. The analysis used Alberta data to forecast the outcomes of changing recommendations to include either annual or biennial screening for ages 45-49 or 40-49. The numbers were projected for a single year cohort followed over their lifetime. The four options were projected and numbers provided in Table 2 show the increase in screens, false positives and cancer deaths averted compared to the status quo (i.e. biennial screening recommended starting at age 50). Outcomes have been standardized to include the same number of Albertans (41,000) receiving screening in each option to allow for comparison of the benefits and harms.

	BIENNIAL 45-49 Y	ANNUAL 45-49 Y	BIENNIAL 40-49 Y	ANNUAL 40-49 Y
Total additional screens	96,000	177,000	141,000	266,000
Additional false positive results	11,000	20,000	16,000	30,000
Cancer deaths averted*	9	13	12	18
Cost per Quality-Adjusted-Life-Years gained†	$41,000 (vs. status quo)	$110,000 (vs. biennial 45-49 Y)	$87,000 (vs. biennial 45-49 Y)	$107,000 (vs. biennial 45-49 Y)

Table 2. Projected clinical impact for a cohort aged 40-49 years in 2021 in Alberta (forecast performed in 2020 and ignored impacts from the COVID-19 pandemic). The outcomes were tracked over the lifetime of each simulated person (i.e. each simulated person was followed until they died to track whether they died of breast cancer or other causes).

Although options such as the annual 40-49 strategy averted 9 more cancer deaths than the biennial 45-49 strategy, it was projected to result in triple the number of additional screens and false positives. Additionally, the projections calculated the healthcare costs and quality-adjusted

*The analysis was conducted using a larger cohort of Albertans (aged 40-49y in Alberta in the next 20 years) and divided the outcomes by 20 because cancer death was a rare outcome.

†Due to data limitations, the false positive rate for ages 40-49 were used for both 40-49y and 45-49y. If the false-positive rates are higher for younger people (40-44y), one would expect the 40-49y screening strategy to have more false-positives and be less cost-effective than the above results.

life-years (QALY) of each strategy. A commonly cited threshold of $50,000 per QALY was used to assess if any of the alternatives were considered cost-effective. Of the four alternatives, only biennial screening starting at age 45 proved cost-effective. Therefore, recommending biennial screening starting at age 45 was considered the best balance of benefits to harms while also being the most cost-effective.

75 Years and Older: There are no studies that demonstrate benefit of screening in people 75 years and older; however, these people are at increased risk for developing breast cancer[61] and may continue to benefit from screening regardless. Healthcare providers should consider individual health factors and the individual's preference to continue screening. If choosing to continue screening, the recommended screening interval in this age category is every 2 years. Patients who have less than 10 years of life expectancy remaining are unlikely to experience meaningful benefit from continued screening.

OTHER SCREENING-RELATED TECHNOLOGY

Practice Point

Digital mammography (2D) remains the standard for screening the average-risk population.

Digital Breast Tomosynthesis (DBT/3D Mammography)

The Canadian Association of Radiologists/Canadian Society of Breast Imaging provides a useful position statement on the utilization of DBT in mammography screening:

Digital breast tomosynthesis (DBT) is a form of serial sectioning created by digital reconstruction of multiple low-dose mammographic projections into contiguous slices. It is often referred to as "tomo" or "three-dimensional" (3D) mammography, although it is not a truly multiplanar form of 3D.[62] Slice thickness may be adjusted depending on the vendor and/or software used for display. Images are obtained in the same plane as the original compression plane and are read as planar images. Tomosynthesis images can be acquired with ("combo-mode") or without standard two dimensional (2D) digital mammography (DM). Synthetic 2D mammograms are 2D projection images reconstructed from the information acquired during DBT data acquisition (post processing). The DBT slices or "stack" must be interpreted alongside the 2D imaging, either standard 2D DM or synthetic mammogram images.[63,64,65]

Moderate-quality evidence indicates that combining DBT with DM improves invasive breast cancer detection by 2 per 1,000 screens.[66] Invasive cancer detection has been found to be significantly higher with DBT in people with heterogeneously dense breasts of all age groups.[61] Likewise, an analysis of two high volume clinics in Alberta found improvement in cancer detection rates, annual return to screen rates, and positive predictive values after switching from DM alone to DBT+DM.[67] However, abnormal call (recall) rates increased. There has also been inconsistency in findings from other studies on the impact DBT has on false positive results.[66]

Evidence on interval cancer, advanced cancer rates and mortality data is still pending. A rapid review in 2019 by the Canadian Agency for Drugs and Technologies in Health (CADTH) found

inconclusive evidence on the clinical benefits or harms of DBT.[68] More recent studies have found early evidence of improved interval cancer rates with DBT.[69,70] DBT also increases the radiation exposure compared with 2D DM alone, but remains within acceptable dose limits (see the section on Radiation Risk).

DBT Recommendation

2D DM remains the standard for screening average-risk individuals. At the present time there is not enough evidence to provide a strong recommendation for or against the use of DBT in the average-risk population. If using DBT for screening, it should be used in conjunction with synthetic or standard 2D DM.

Ultrasound: Ultrasound should not be used as a stand-alone screening test. There is insufficient evidence to support the use of ultrasound for routine screening in the average-risk population. Evidence to date shows that the addition of ultrasound to mammography can detect an additional 3.8 cancers (mostly invasive) per 1,000 people with dense breasts;[71] however, it also produces significantly more false positives.[72] The balance of benefits and harms of supplemental ultrasound is greater for people with category D (extremely dense) breasts, as denser breasts tend to mask abnormalities.[71,73] It is for this reason that we recommend considering annual breast ultrasound, in addition to mammography, for people with extremely dense breast (category D) for ages 45+.

Magnetic Resonance Imaging (MRI): To date, MRI screening studies have focused on the high risk population; there are limited studies evaluating the use of MRI for screening in the average-risk population.[40] Some preliminary studies suggest that abbreviated or fast MRI could improve cancer detection for average-risk people with dense breasts (category C or D), but further research is needed on its cost-effectiveness and impact on reducing breast cancer mortality.[74,75]

Thermography: Breast thermography is not approved by Health Canada for use in breast cancer screening. There is no evidence that thermography reduces mortality related to breast cancer.[76,77] It may lead to a false sense of security and potential harm. People should be discouraged from using thermography for the detection of breast cancer.

OTHER SCREENING RELATED APPROACHES

Clinical Breast Exam (CBE): The addition of CBE to screening mammography has not been proven to reduce mortality. Although some cancers may be identified by CBE,[78] there is no evidence that CBE results in fewer deaths. Additionally, CBE is not specific and generates a significant number of false positive results.[79] Expert opinion recommends that CBE be considered (particularly for individuals at higher-than-average risk or high-risk) as part of the physical examination and as a teaching opportunity to discuss breast awareness (see below).

Breast Awareness (BA): BA means being familiar with one's own breasts. Any unusual changes should be reported to their healthcare provider; in particular, nipple discharge/rash/inversion, skin dimpling, or new mass in the breast or axilla.[80]

For a visual graphic that patients can use to help become breast aware, visit: screeningforlife.ca/breast/breast-cancer/#signs_and_symptoms

Breast Self Exam (BSE): BSE is the practice of regularly checking one's own breasts for signs of cancer. It has not been shown to be beneficial for early detection of breast cancer; additionally, no major guidelines currently recommend it for screening. Instead, individuals should be encouraged

to practice BA.

Remember, no test is perfect. Persistent or new changes should be followed up by the healthcare provider, even if recent investigations were normal.

Breast Cancer Screening for Individuals at Higher-than-Average Risk

Higher-than-average risk is a new category to these guidelines. It has been added to address several risk factors that do not qualify as high risk. Definitions of higher-than-average risk vary between guidelines and within the literature, but it is commonly described as people with a 15 to 20% lifetime risk of developing breast cancer.[34,81,82] Alternatively, several guidelines define higher-than-average risk according to specific criteria.[83,84] Expert opinion is that the use of pre-defined criteria to define this group can be more straightforward to follow, and is independent of the risk assessment model available; it is also more practical for implementing in a day-to-day healthcare setting since it doesn't require working through a risk assessment tool during a time-restricted visit.

Breast Cancer Screening for Individuals at High Risk

The recommendations for the high risk population were developed in response to feedback from family physicians requesting guidance for people requiring more intensive screening or surveillance, and also for people requiring referral to medical genetics.

Recommendations are based on best evidence. Program considerations developed by an expert panel from medical genetics and high risk assessment clinics in Calgary and Edmonton and are consistent with other published guidelines. See Appendix A for referral criteria for genetic testing. See Appendix B for referral to high-risk assessment/management clinics.

SUGGESTED CITATION

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For more information see www.screeningforlife.ca

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Appendices

Appendix A

REFERRAL TO MEDICAL GENETICS

Individuals with a personal and/or family history **(maternal or paternal)** meeting the referral criteria below should be referred to Medical Genetics for potential counselling and genetic testing. Below are the referral criteria. Criteria are updated periodically so check with the clinic for the most up to date referral form.

SUGGESTED REFERRAL CRITERIA FOR GENETICS CLINICS

Relatives of an individual with a confirmed pathogenic or likely pathogenic mutation in a breast or ovarian cancer (HBOC) gene.

BREAST CANCER

1. Personal history of breast cancer diagnosed ≤ 35.§
2. Personal history of bilateral breast cancer; both diagnosed < age 60.§
3. Personal history of breast and ovarian cancer*.§
4. Personal history of breast and pancreatic cancer.§
5. Personal history of breast cancer ≤ 50 AND a family history of breast cancer ≤ 50.
6. Personal history of breast cancer AND family history of ovarian cancer* diagnosed at any age.
7. Personal history of breast cancer AND two family members with breast cancer; one diagnosis ≤ 50.
8. Personal history of breast cancer AND two family members with pancreatic adenocarcinoma at any age.
9. Personal history of triple negative breast cancer (ER-ve, PR-ve, Her2-ve) diagnosed ≤ age 65.§
10. Personal history of male breast cancer diagnosed at any age.§
11. Personal history of breast cancer and family history of male breast cancer.
12. Personal history of breast cancer at any age and a first degree relative meeting a [§] criterion.
13. Ashkenazi Jewish heritage and personal history of breast or ovarian cancer* at any age.
14. Ashkenazi Jewish heritage and a 1st or 2nd degree relative with breast/ovarian cancer* at any age.

*Ovarian cancer = invasive epithelial ovarian cancer, and includes primary peritoneal cancers and primary fallopian tube cancers.
§ = Mainstreaming criteria; patient meeting these criteria can have genetic testing ordered through approved surgeon/oncologist.

MEDICAL GENETICS CLINICS

CALGARY

Hereditary Cancer Clinic
Alberta Children's Hospital
28 Oki Drive NW
Calgary, Alberta T3B 6A8

403-955-7373, 403-955-7137 (Booking)
albertahealthservices.ca/info/page15513.aspx

Referral form: albertahealthservices.ca/frm-20089.pdf

> Alberta Referral Directory

EDMONTON

Hereditary Cancer Clinic
Stollery Children's Hospital/University of Alberta Hospital
8440 112 Street
Edmonton, Alberta T6G 2B7

780-407-7333, 780-407-7336
albertahealthservices.ca/info/page15513.aspx

Referral form: albertahealthservices.ca/frm-20042.pdf

> Alberta Referral Directory

Appendix B

REFERRAL TO HIGH RISK ASSESSMENT/MANAGEMENT CLINICS

These clinics are to recommend appropriate screening and prevention strategies for women already diagnosed as high risk.

Options for finding a clinic in your area:

- Alberta Referral Directory: allows you to search for a breast health program in your area
- Provincial Breast Health Referral Quick Reference: regional referral information for breast health

CALGARY

Calgary Breast Health Program
Women's Health Centre
Suite 187, 1403 29 Street NW
Calgary, Alberta T2N 2T9

403-944-2240

ahs.ca/cbhp

> Alberta Referral Directory

REFERRAL CRITERIA

1. Genetic Risk for Breast +/- Ovarian Cancer

- Known BRCA gene mutation (or other gene mutation associated with increased breast cancer risk) in self or first degree relative and interested in further discussion regarding screening and prevention strategies. (include medical genetics letter)
- High risk for breast or ovarian cancer as already assessed by a Cancer Genetics Clinic (i.e. strong family history but BRCA negative family or genetic testing not desired) and interested in further discussion regarding screening and prevention strategies.

2. Elevated Breast Cancer Risk Due to Another Reason

- Atypical hyperplasia or lobular carcinoma in situ of the breast and is interested in learning about screening recommendations and risk reduction hormonal therapies (i.e. Tamoxifen, raloxifene, exemestane.)
- Radiation treatment to the chest area before age 30.

EDMONTON

Allard HBOC Clinic Edmonton
Room 250, 2nd Floor, West Wing
Community Services Centre
10240 Kingsway Ave.
Edmonton, Alberta T5H 3V9

780-735-4718

Programs & Services

> Alberta Referral Directory

- Provides care for women who have a high risk of hereditary breast and ovarian cancer.
- Patients must be referred to the clinic by a physician.

REFERRAL CRITERIA

Patients age 25 to 70 and have not had bilateral mastectomies (exception GyneOncology only referral) and one of the following:

- Patients who are **recommended** for follow up by a **Genetics Clinic** (with >20% lifetime risk)
- Patients who have a mutation associated with an increased risk of breast cancer
- **Relatives** of patients who have a documented **mutation in a breast cancer associated gene**
- Family members of patients in the clinic who have a recommendation by HBOC clinicians
- Women with history of **radiation treatments to the thorax** before the age of 30

Strong family history of breast and/or ovarian cancer on *same side* of family:

Two family members with breast cancer if:

- One has been diagnosed with bilateral breast cancer
- One is male
- Both people were diagnosed with breast cancer under the age of 50

- Three family members with breast cancer one of whom is under the age of 50 (this may span two generations)
- Four family members with breast cancer
- A single individual who has had breast cancer and a confirmed ovarian cancer* (either first degree relative or paternal aunt)
- A diagnosis of breast cancer and confirmed ovarian cancer* on the same side of the family.

Note: Family members should be blood relations to each other and the referred patient.

*Ovarian cancer refers to invasive non-mucinous epithelial ovarian cancer, includes cancer of the fallopian tubes or primary peritoneal cancer, excludes borderline or low malignant potential ovarian tumor.

Appendix C

EXPOSURE DEFINITIONS FOR MODIFIABLE ATTRIBUTABLE RISKS FOR BREAST CANCER

RISK FACTOR	EXPOSURE DEFINITION
Smoking	Current smoker (smoked cigarettes daily or occasionally at the time of the interview) or former smoker (did not smoke at the time of the interview and had smoked more than 100 cigarettes in lifetime)
Passive smoking	Regularly exposed to tobacco smoke in their home, a vehicle or a public place
Physical Inactivity	Moderately inactive: daily energy expenditure based on leisure time physical activity is ≥1.5 and <3.0 kcal/kg/day Inactive: daily energy expenditure based on leisure time physical activity is <1.5kcal/kg/day
BMI	Body mass index (BMI) ≥25 kg/m2
Sedentary	Sedentary ≥6 hours per day during leisure time
Alcohol	Having any number of drinks per day (13.5g of ethanol per drink)
Low fruit	Less than 4 servings a day
Shiftwork	Having a work schedule of rotating shifts (including nights) or of permanent night shifts, as defined by CAREX Canada estimated based on the Survey of Labour and Income Dynamics (SLID) 1996

Appendix D

CLINICAL PRACTICE GUIDELINE COMMITTEE MEMBERS

NAME	POSITION	ORGANIZATION	CONFLICT OF INTEREST DISCLOSURE
Voting Members			
Dr. Shiela Appavoo	Radiologist	Alberta Society of Radiologists	Affiliation with not-for-profit organization: ·CSBI Scholarly work: ·CAR/CSBI Breast Imaging guideline, density position statement ABCCSP, 2019 Highlights in Medicine University of Saskatchewan Other: ·Practicing mammography reader
Dr. Jane Baker	Family Physician	University of Alberta – Department of Family Medicine	Affiliation with not-for-profit organization: ·Edmonton Oliver PCN and University of Alberta ·Practicing Family Physician
Dr. Bernice Capusten	Radiologist	Alberta Society of Radiologists	Affiliation with not-for-profit organization: ·Alberta Society of Radiologists Scholarly work: ·Journal CAR, ASR meeting presenter
Dana Dudar	Mammography/ Quality Control Technologist	Alberta Health Services – Screen Test	Affiliation with not-for-profit organization: ·AHS Employee
Dr. Tracy Elliot	Radiologist	Alberta Society of Radiologists	Other: ·Practicing mammography reader
Dr. Karla Gustafson	Medical Officer of Health	Alberta Health Services	Affiliation with not-for-profit: ·AHS Employee

NAME	POSITION	ORGANIZATION	CONFLICT OF INTEREST DISCLOSURE
Dr. Sasha Lupichuk	Medical Oncologist	Cancer Control Alberta – Tom Baker Cancer Centre	Affiliation with for-profit organization: ·Novartis, AstraZeneca, Roche Odonate Therapeutics Affiliation with not-for-profit organization: ·AHS Cancer Control, National Cancer Institute of Canada
Sue Peters	Public Representative	N/A	Affiliation with not-for-profit organization: ·Health Quality Council of Alberta, Alberta Medical Association
Joanne Stewart	Nurse Practitioner – Family	Alberta Health Services	Affiliation with not-for-profit organization: ·Northern Alberta Home for Women Society and University of Alberta ABSPORU
Dr. Lisa Stevenson	Committee Co-Chair, Family Physician	Clinical Assistant Professor – Department of Family Medicine at the University of Calgary	Affiliation with not-for-profit organization: ·Canadian Digestive GI clinical pathways, Health SCN/AHS subcommittee ·Practicing Family Physician ·Calgary West Central Primary Care Network ·University of Calgary
Dr. Glen Vajcner	Surgeon	Alberta Health Services	Affiliation with not-for-profit organization: ·MIL for AHS, Clinical Lecturer UofA

NAME	POSITION	ORGANIZATION	CONFLICT OF INTEREST DISCLOSURE
Dr. Huiming Yang	Committee Co-Chair, Medical Director	Alberta Breast Cancer Screening Program	Affiliation with not-for-profit organization: ·AHS Employee Scholarly Work: ·Numerous
Non-Voting Members			
Janell Bryant	Translation Services	Alberta Breast Cancer Screening Program	N/A
Bonnie Chiang	Manager	Alberta Breast Cancer Screening Program	N/A
Seema Mutti-Packer	Translation Services	Alberta Breast Cancer Screening Program	N/A
James Newsome	Program Coordinator	Alberta Breast Cancer Screening Program	N/A
MaryAnne Zupancic	Consultant	Accelerating Change Transformation Team	N/A
External Reviewers			
Dr. Antoine Bouchard-Fortier	Surgeon	Alberta Health Services	Affiliation with not-for-profit organization: ·AHS, University of Calgary
Dr. Heather Bryant	Chief Scientific Officer	Canadian Partnership Against Cancer	Affiliation with not-for-profit organization: ·Alberta Cancer Foundation, Canadian Partnership Against Cancer
Dr. Jeffrey Cao	Radiation Oncologist/ Provincial Breast Tumour Team Lead	Tom Baker Cancer Centre/ Alberta Health Services	Affiliation with for-profit organization: ·Pfizer, Novartis, AstraZeneca Affiliation with not-for-profit organization: ·Canadian Radiation Oncology Foundation and Canadian Association of Radiation Oncology

NAME	POSITION	ORGANIZATION	CONFLICT OF INTEREST DISCLOSURE
Dr. James Dickinson	Professor of Family Medicine and Community Health Sciences	University of Calgary	Affiliation with not-for-profit organization: ·Fluoride Yes Scholarly Work: ·Canadian Family Physician and Family Medicine Forum 2019
Gregory Doyle	Chair	Canadian Breast Cancer Screening Initiative	Affiliation with not-for-profit organization: ·Numerous (examples: Canadian Partnership Against Cancer, Canadian Translational Advisory Committee Scholarly Work: ·Numerous
Jennifer Koppel	Nurse Practitioner	Alberta Health Services	Affiliation with not-for-profit organization: ·AHS Employee
Dr. Bettina Lott	Family Physician	N/A	Affiliation with not-for-profit organization: ·Sherwood Park PCN, AHS, UofA
Dr. Colin Mar	Medical Director	BC Cancer Breast Screening	Affiliation with not-for-profit organization: ·B.C. Cancer Breast Screening, Provincial Health Services Authority
Dr. Laura McDougall	Senior Medical Officer of Health/ Senior Medical Director	Alberta Health Services	Affiliation with not-for-profit organization: ·AHS, University of Calgary
Dr. Derek Muradali	Radiologist	University of Toronto	Affiliation with not-for-profit organization: ·Canadian Partnership Against Cancer
Dr. Elizabeth Ngan	Radiologist	Alberta Health Services – Screen Test	Affiliation with not-for-profit organization: ·Cross Cancer Institute Medical Imaging Consultants, University of Alberta, Alberta Health Services

For more information, contact the Alberta Breast Cancer Screening Program at abcsp@ahs.ca

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