Colin Mar, MD, FRCPC, Janette Sam, RTR, Christine Wilson, MD, FRCPC

Breast cancer screening in British Columbia: A guide to discussion with patients

Primary care providers have an important role to play in helping their patients consider the benefits, limitations, and downsides of screening mammography.

ABSTRACT: Breast cancer continues to affect the women of British Columbia and impose a significant health care burden. Population-based screening mammography remains the most accessible and scientifically validated test for detecting breast cancer and reducing breast cancer mortality. Screening is provided across the province by the Screening Mammography Program of BC. Downsides of screening include exposure to ionizing radiation, false-positive results, and overdiagnosis. Current screening policy in BC is based on age and other determinants of risk, including family history and genetic factors. For example, routine screening every 2 years is recommended for asymptomatic women age 50 to 74 of average risk, while routine screening every year is recommended for women age 40 to 74 with a first-degree relative with breast cancer. The Screening Mammography Program compiles data for calculating numerous outcomes, including participation and return rates, time to diagnosis measures, and sensitivity and specificity indicators. Breast density is an issue a woman and her primary care provider may need to consider, since normal dense breast tissue may impede detection of cancer. Imaging technologies undergoing investigation to address this and other challenges include digital breast tomosynthesis, ultrasound, and magnetic resonance imaging (MRI). By discussing imaging options and screening benefits, limitations, and downsides with women, primary care providers can facilitate informed decision making.

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The potential impact of breast cancer on women in British Columbia means that primary care providers should be prepared to address the female patient's question, "Should I get a mammogram?" It can be helpful to begin with a brief review of some principles of screening from the classic World Health Organization report by Wilson and Jungner:

- The condition sought should be an important health problem.
- There should be an available treatment.
- There should be an acceptable test.[1]

These principles have undergone multiple revisions over the years and additional criteria have been proposed, including:

- There should be scientific evidence

Dr Mar is the medical director of the Screening Mammography Program of BC and a clinical assistant professor in the Department of Radiology at UBC. Ms Sam is the operations director of the Screening Mammography Program of BC. Dr Wilson is the director of breast imaging at BC Cancer in Vancouver and a clinical associate professor in the Department of Radiology at UBC.

of screening program effectiveness.
- There should be quality assurance.
- The overall benefits of screening should outweigh the harm.[2]

Although breast cancer screening, treatment, and surveillance in BC have contributed to outcomes matching national and international standards,[3] the disease remains the most common cancer in women in Canada, and the second leading cause of cancer death as of 2015.[4] In 2010 the lifetime risk for developing breast cancer was 1 in 9 and the lifetime mortality risk was 1 in 30. Since 1986 there has been a steady decline in the age-standardized breast cancer mortality rate, which now stands at 16 per 100 000 in BC. The age-standardized 5-year relative survival ratio for 2006 to 2008 was 88% across the country.[4]

Population screening for breast cancer in BC began in 1988 with the Screening Mammography Program (SMP). There are SMP centres located in all five health authorities, with 36 fixed sites across the province and three mobile units providing access for remote and underserviced regions. The program is completing a transition to digital mammography, which facilitates the transfer of images between centres, and has been shown to improve cancer detection in younger women and those with dense breast tissue.[5]

Evidence for screening mammography

The evidence for breast cancer screening with mammography has engendered much discussion. Several randomized controlled trials were conducted prior to 2000 and meta-analyses of these demonstrated reductions in breast cancer mortality with screening of RR 0.80 to 0.82.[6-8] These studies may, however, underestimate the current effectiveness of screening given their age and use of intention-to-treat analysis. Mammography technology has evolved since 2000, and quality assurance programs have been developed. Observational studies have yielded more recent data. These include the work of Coldman and colleagues, who considered over 2 million women age 40 to 79 in 7 of 12 Canadian screening programs during the period 1990 to 2009,[9] and observed a 40% mortality reduction, with little variation by age. The number needed to participate in screening to prevent a single breast cancer death within 10 years decreased with age from 1247 for women first screened at age 40 to 49, to 498 for women first screened at age 70 to 79.

The Canadian Task Force on Preventive Health Care (CTFPHC) last issued guidelines for breast cancer screening in 2011.[7] These included a weak recommendation for mammography every 2 to 3 years for women age 50 to 69, and the same for women 70 to 74. Evidence of similar quality supporting a weak recommendation for mammography for women age 40 to 49 was reported, but a recommendation was not provided after the CTFPHC cited a less favorable benefit-to-harm ratio in this age group.

A working group of the International Agency for Research on Cancer (IARC) subsequently published an evidence review in 2015.[10] They concurred with the CTFPHC in that they found sufficient evidence to recommend screening for the 50 to 69 and 70 to 74 age groups. They were, however, unable to find sufficient evidence to make a recommendation for women 40 to 49, citing fewer studies for this age group.

The American Cancer Society (ACS) released a guideline update in 2015[11] that included a strong recommendation for regular screening mammography starting at age 45 and a qualified recommendation for annual screening for women 45 to 54. The ACS update also included qualified recommendations for biennial screening beginning at age 55, and continued screening at 70 to 74 to be based on life expectancy. Finally, the update included a qualified recommendation that women "should have the opportunity to begin annual screening between the ages of 40 and 44 years." Since a qualified recommendation indicates "there is clear evidence of benefit, but less certainty about either the balance of benefits and harms, or about patients' values and preferences,"[11] different patients offered this opportunity will make different decisions and discussion will be required. In these cases, the primary care provider has an important role to play in facilitating informed decision making.

None of the three organizations has found sufficient evidence to support a recommendation for routine clinical breast examination or breast self-exam. The American Cancer Society has suggested that the time required for clinical breast examination instead be used for discussion of the benefits, limitations, and downsides of mammography.

Downsides of screening mammography

As noted previously, a discussion of screening requires considering downsides. These include exposure to ionizing radiation, patient anxiety, false-positives, and overdiagnosis.

The radiation risk posed by current standards in digital mammography is low. For a woman undergoing mammography at age 40, the estimated lifetime attributable risk (LAR) of a fatal breast cancer is 1.3 cases per 100 000. Continuation with annual mammography to the age of 80 is associated with an LAR of 20 to 25 cases.[12] The IARC included a statement in its 2015

guidelines that the risk of radiation-induced malignancy is outweighed by the benefits of mammography.[10]

False-positives in screening mammography are inherent to the practice. In 2015 the positive predictive value in the SMP for first screens was 5.2% and for subsequent screens was 7.0%, values that both met national targets.[13] Anxiety caused by false-positives is related to receiving notification of an abnormal result and undergoing consequent image-guided or surgical biopsy. Such anxiety has been documented,[14] but has not been found to have a measurable health utility decrement.[15] There are also varying morbidity and risks associated with different biopsy procedures. Overdiagnosis involves the detection by mammography of a malignancy that would never have become clinically apparent before the patient's death. The issue then is one of results that precipitate overtreatment. The measurement of this is complicated, primarily by uncertainty regarding the true incidence of breast cancer, the subject of much discussion and debate. Recently published overdiagnosis rates range from 2.3% in a Danish population-based cohort study[16] to 48.3% in a later Danish study that included findings for invasive cancer and ductal carcinoma in situ (DCIS).[17] A retrospective study of provincial SMP data estimated rates of 5.4% for invasive cancer and 17.3% when DCIS was included, with the risk of overdiagnosis being highest in older women.[18] In discussing this issue with patients it remains important to recognize that the lifetime risk for overdiagnosis is low, in the order of 1.0%.[19] Moreover, it is not currently possible at the time of diagnosis to distinguish between tumors that will not progress from those that will. The decision will therefore be based on the patient's tolerance of the relative risks.

BC screening policy

Population screening recommendations for breast cancer in BC are categorized by age and other determinants of risk, including family history and genetic factors (**Table**). Women eligible for screening are asymptomatic, without a personal history of breast cancer, and without breast implants. Women age 40 to 49 are encouraged to consider the benefits relative to the downsides and limitations in discussion with their primary care provider. A limitation for women in this age group, where the incidence of cancer is lower than in older age groups, is the greater prevalence of dense breast tissue that may impede cancer detection.[20]

For women at high risk due to a genetic predisposition or a history of chest wall irradiation between the ages of 10 and 30 years, screening MRI is recommended in addition to annual mammography, although MRI is not provided through the SMP.

Regarding clinical breast examination, there is no recommendation for or against this practice in asymptomatic women. Finally, the policy recommends against breast self-examination as an alternative to mammography.

Table. Screening Mammography Program of BC guidelines for primary care providers.

Physician Protocol for Screening Mammograms

RISK	POLICY
Average risk **Ages 40-49**	Health care providers are encouraged to discuss the benefits and limitations of screening mammography with asymptomatic women in this age group. If screening mammography is chosen, it is available every **two years**. Patients will be recalled every two years.
Average risk **Ages 50-74**	Routine screening mammograms are recommended every **two years** for asymptomatic women at average risk of developing breast cancer. Patients will be recalled every two years. A health care provider's referral is not required.
Average risk **Ages 75+**	Health care providers are encouraged to discuss the benefits and limitations of screening mammography with asymptomatic women in this age group. Health care providers should discuss stopping screening when there are comorbidities associated with a limited life expectancy or physical limitations for mammography that prevent proper positioning. If screening mammography is chosen, it is available every **two to three years**. Patients will not be recalled by the Screening Mammography Program of BC.
Higher than average risk **Ages 40-74 with a first degree relative with breast cancer**	Routine screening mammograms are recommended **every year**. Patients will be recalled every year. A health care provider's referral is not required.
High risk **With a known BRCA1 or BRCA2 mutation or prior chest wall radiation or strong family history of breast cancer**	Age 40-74: please refer to recommendation for "Higher than average risk" women. Under age 40: The Screening Mammography Program accepts women at high risk of developing breast cancer **with a health care provider's referral**, provided they do not have breast implants or an indication for a diagnostic mammogram.

Source: BC Cancer

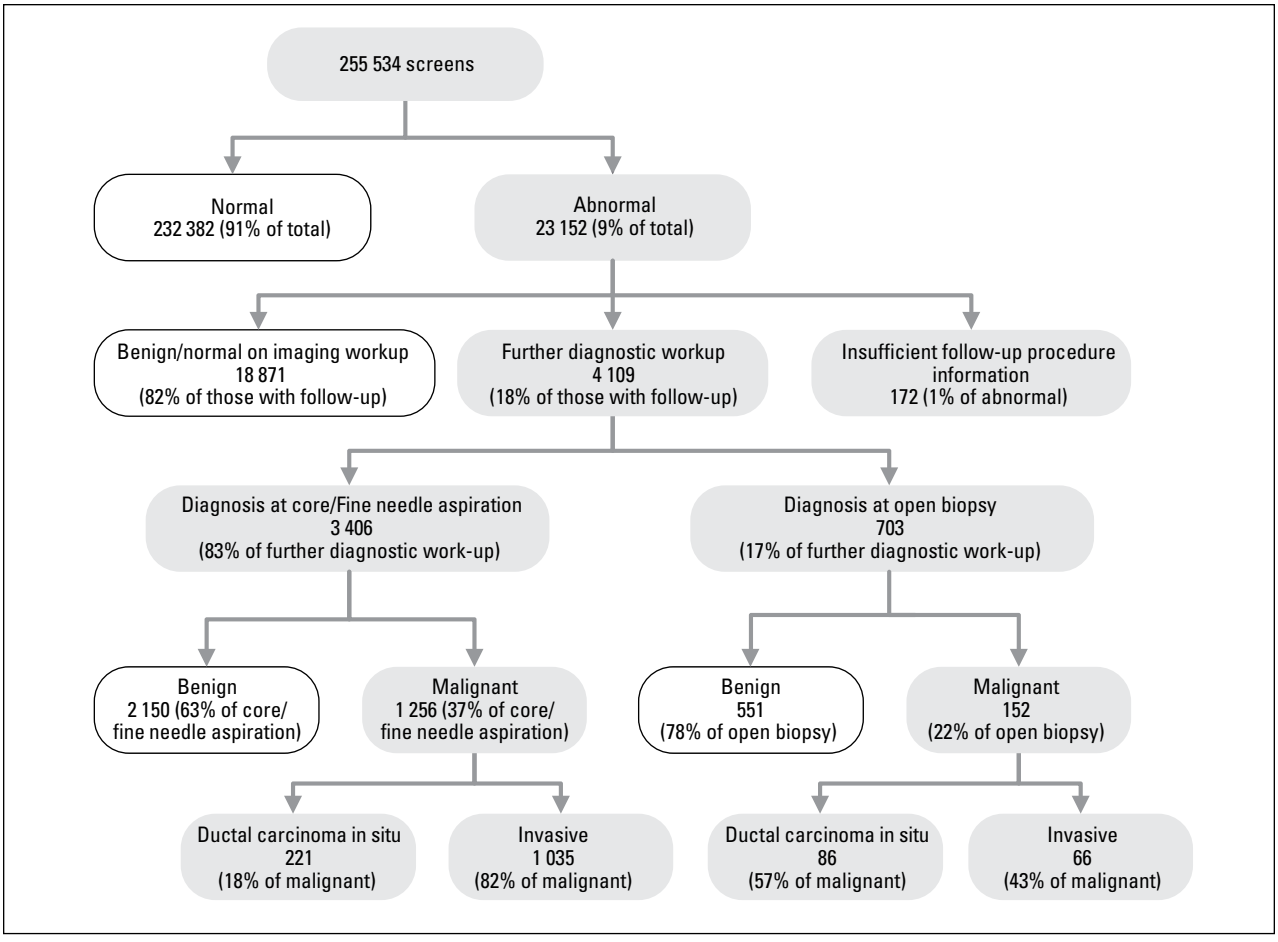

Figure 1. Breast cancer screening outcomes, 2015.[13]

Source: BC Cancer

Screening program outcomes

Objective outcome measures are integral to quality assurance in a screening program. The SMP compiles data for calculating numerous outcome measures that are then shared in a variety of ways. The program's annual report is the most comprehensive of these, and may be accessed at www.bccancer.bc.ca/screening/Documents/SMP_Report-AnnualReport2016.pdf. The report includes participation and return rates, time to diagnosis measures, and sensitivity and specificity indicators, and compares these indicators to national standards where available. The program also considers participation by region and by selected ethnic groups.

In 2015 the provincial participation rate for women age 50 to 69 was 52.4%, a rate that has remained both relatively stable and below the national target of 70.0% since 2000.[13] Participation rates by women age 50 to 69 in the Northeast health service delivery area (40.0%) and Kootenay Boundary health service delivery area (44.0%) were below the provincial average. Data were compiled for clients identified as First Nations, East/South East Asian, and South Asian. The participation of women within the same age range in all three groups rose over the previous 5 years, and lies above the provincial average. This interpretation may, however, be limited by underestimation of the ethnic group populations.[13]

More than 250 000 mammograms were performed by the SMP in 2015. Screening outcomes considered included normal and abnormal results, image-guided and surgical biopsies performed, and breast cancers detected (**Figure 1**). The percentage of women referred for further testing because of an abnormal screening mammogram (i.e., the abnormal call rate) was 9.1%. The number of women with a screen-detected cancer per 1000 women who had a screening mammogram (i.e., the cancer detec-

tion rate) was 5.5. The percentage of women with an abnormal mammogram who were diagnosed with breast cancer (i.e., the positive predictive value) was 6.1%.[13]

In addition to the outcome measures already noted, individualized data are compiled for each radiologist screener in the program and for each provincial health authority. The SMP also promotes quality assurance through a client satisfaction survey sent to selected women attending program sites across the province. Each SMP site and radiologist maintains mammography-specific accreditation from the Canadian Association of Radiologists. This requires adherence to a nationally recognized set of guidelines that ensures the quality of the examination and the competence of the screener. Finally, specific policies regulate the systematic review of randomly sampled abnormal findings and cancers diagnosed. This occurs at both the site level to facilitate direct feedback and at the program level to ensure overall effectiveness.

Breast density

Risk stratification in the current SMP screening policy is based primarily on age and family history, but another factor a woman and her primary care provider should consider is breast density. This is a measurement of the proportion of the breast composed of dense (i.e., nonfatty) tissue, and the probability of masking a cancer. Dense tissue is relatively radiopaque and thus appears white on a mammogram. Although normal, such tissue may obscure cancer and thus impede its detection.[20] A set of mammograms (**Figure 2**) illustrates the difference between dense and nondense breasts, and how cancer may resemble dense tissue. Given this masking effect, any breast changes or symptoms should be followed up, regardless of a normal screening mammogram result.

Breast density is also a risk factor for incident cancer, particularly when the breast is extremely dense. A meta-analysis in 2006 considered over 14 000 breast cancer cases with 226 000 controls to determine a 4.64-fold risk when the proportion of dense to non-dense breast tissue was equal to or greater than 75%,[21] relative to a breast of less than 5%. Breast cancer in the setting of dense breast tissue has not, however, been associated with an increased risk of death.[22]

The reporting of breast density with mammogram results has been the focus of much recent discussion. As of early 2016, 24 American states have enacted legislation that mandate this reporting.[23] While there is no legislative requirement in Canada to report on breast density, the SMP policy on reporting of breast density is currently under review. For now, the information is available upon patient request, with the understanding that this risk factor should not be considered in isolation, but in combination with age, family history, and other risk factors.[24] At this time, there have been no guideline revisions regarding supplemental screening for women with dense breasts.

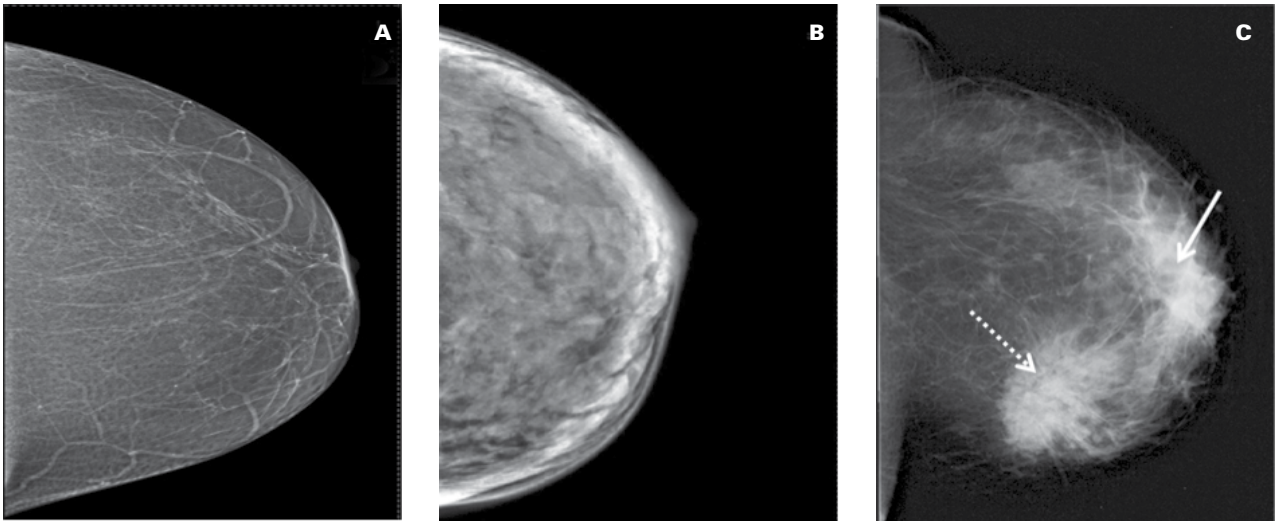

Figure 2. Mammograms illustrating the challenge breast density may pose in their interpretation. A: Low opacity seen in non-dense breast with a high proportion of fat. B: Increased opacity seen in a dense breast. C: Opacity seen in both normal dense breast tissue (solid arrow) and adjacent cancer (dashed arrow).

Emerging technologies

Mammography remains the most accessible and scientifically validated test for breast cancer screening, and the sole modality included in guidelines for women of average risk. It is, however, helpful to have a basic understanding of some of the other breast imaging modalities that are the focus of ongoing research, and may arise in discussion with patients.

Digital breast tomosynthesis (DBT) is commonly referred to as the 3-D mammogram. Indeed, this examination utilizes the technology of mammography to produce a series of two-dimensional images of a single breast. These are acquired through an arc trajectory, and ultimately viewed as a three-dimensional image set. Multiple studies have demonstrated the ability of DBT to increase cancer detection while decreasing the rate of patient recall for further evaluation.[25] A prospective trial integrating 2-D and 3-D mammography to screen over 7000 women in 2013 found an additional 2.7 cancers were detected per 1000 screens, and false-positives were reduced by an estimated 17.2%.[26] Two sites within the SMP are currently participating in a large multicentre trial to evaluate the role of DBT in screening.

Ultrasound is integral to breast imaging in the diagnostic setting, and its role in screening is evolving. It is of particular interest in the context of dense breast tissue. An earlier prospective multicentre trial followed women over three rounds of annual mammography with and without supplemental ultrasound. Inclusion criteria were a breast density of at least 50% and at least one other risk factor, such as a personal history of breast cancer. An additional 3.7 cancers per 1000 screens were detected, but with a false-positive rate of 16%.[27]

SMP screening policy indicates the use of MRI for high-risk women with genetic or familial risks or prior mantle radiation exposure. MRI has demonstrated high sensitivity for detecting breast cancer, but the use of this modality is limited by examination time and geographic availability. Recent evaluation of abbreviated imaging protocols for this modality may, however, eventually allow its use for other risk categories by increasing access through shortened time required per visit.[28]

Other imaging modalities such as thermography and nuclear medicine tests, including positron emission tomography, have not been validated for population screening.

Facilitating an informed decision

By increasing awareness of risk factors for breast cancer, the SMP hopes to help women in BC age 40 and older make an informed decision about screening mammography. When researchers analyzed provincial screening data for over 2 million women age 40 to 74 screened between 2000 and 2009, they found decreased false-positives and increased cancer detection with increasing age, and increased cancer detection with a positive family history. The main factors associated with false-positives were time since last screening and a previous false-positive.[29] These and other findings were used to develop the online Breast Cancer Screening Decision Aid of BC Cancer (http://decisionaid.screeningbc.ca), which generates a response after a user answers six questions, including "How old are you?," and "When was your last screening?" The response indicates the likelihood of three events: having a breast cancer found, having a false-positive mammogram, and having a false-positive biopsy. The user is then advised to print the response "and discuss with your doctor to determine if screening is right for you." Research within the program is now underway to consider the roles of both breast density and ethnicity within BC and Canada, and this may further individualize the assessment of risk.

Summary

Both population-based screening and treatment advances have improved breast cancer outcomes. This disease, however, continues to impose a significant burden on the health of women across Canada.[4] Mammography remains the most scientifically validated screening test to reduce breast cancer mortality. A woman's participation in a mammography screening program is best predicated on an informed decision. This requires considering risk factors and understanding the limitations and downsides of screening.

We encourage the public to use the Breast Cancer Screening Decision Aid discussed above and to access resources for general information on screening (www.screeningbc.ca). We also encourage primary care providers to take advantage of the continuing professional development resources available (http://ubccpd.ca/course/bca-screening-update).

Breast cancer screening policy in BC will continue to evolve through ongoing internal data analysis, appraisal of the medical literature and review of working group guidelines that address risk factors such as breast density, and the development of other breast imaging modalities. BCMJ

Competing interests

None declared.

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