



Hôpital général juif
Jewish General Hospital
Centre du cancer Segal Cancer Centre

BREAST CANCER SCREENING

Guidelines for Average and High Risk Patient Populations

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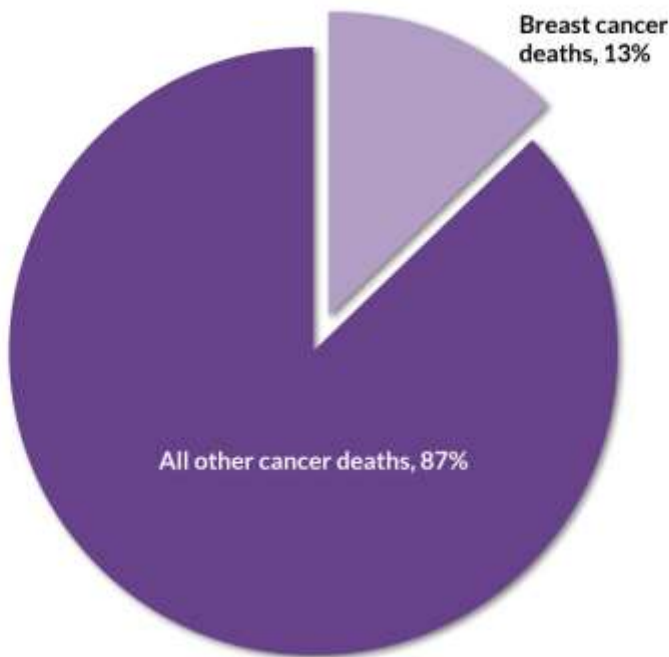
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BREAST CANCER SCREENING

No disclosures except that I am
a breast surgical oncologist.

- Breast cancer is the most common cancer in women worldwide and the second most common cause of cancer related death
 - 26,900 CDN women are diagnosed annually
 - 5,000 CDN women die each year from breast CA
- Mortality from breast cancer has decreased over the last two decades due to both early detection and improvements in systemic therapy

Percentage of All Estimated Cancer Deaths
in Women in 2019



© Canadian Cancer Society

Canadian Cancer Society:
*“Approximately 1 in 8
Canadian women will develop
their breast cancer during
their lifetime and 1 in 33 will
die from it.”*

...But important to remind
ourselves that most women
with breast cancer will not die
from their disease.

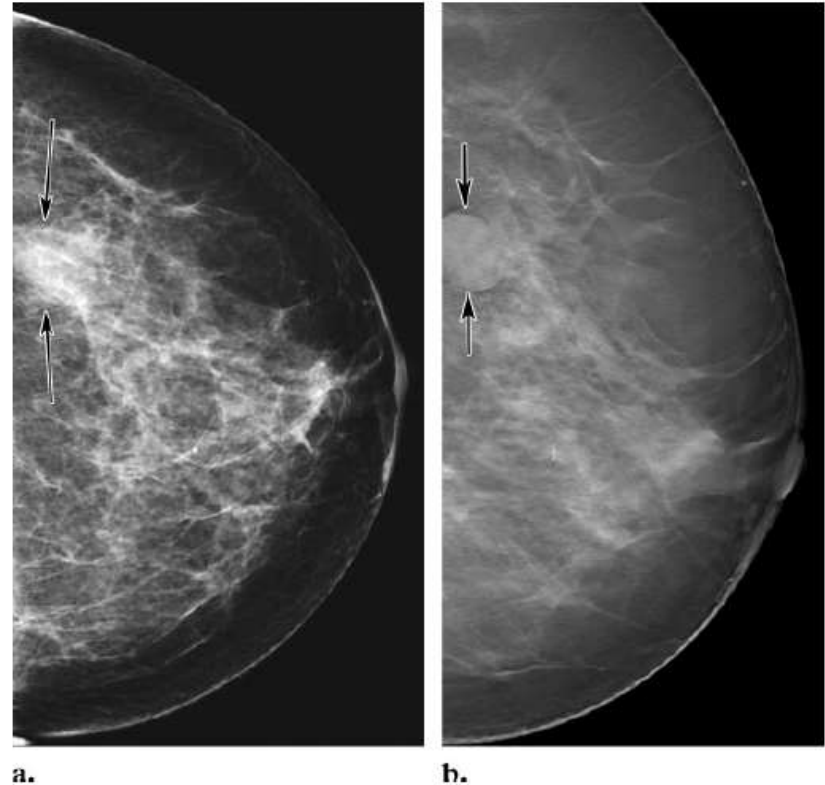
Screening Mammography

- Two 2D views taken of each breast to allow the radiologist to localize an abnormality to a quadrant
 - CC (Craniocaudal) View
 - MLO (Medial Lateral Oblique) View
- BI-RADs system used to describe and classify findings by degree of suspicion
- Callbacks subject to further compression views or magnification views +/- US

Breast Imaging, Reporting, and Data System Category	Assessment and Recommendation
0 - Incomplete	Need additional imaging or prior studies
1 - Negative	Resume routine screening mammography
2 - Benign	Resume routine screening mammography
3 – Probably Benign (<2% risk of malignancy)	Short-term interval follow up at 6, 12, 24 months recommended
4 – Suspicious (3-95% risk of malignancy)	Intermediate risk of malignancy; A)
5 – Highly Suggestive of Malignancy (>95%)	Very high likelihood of malignancy

Tomosynthesis (3D MG)

- FDA approved in 2011
- 3D views of the breast with images acquired at multiple angles and viewed as sequential sections to reduce tissue overlap¹
- Population-based Screening with Tomosynthesis or Standard Mammography (STORM) study²
 - 34% increase in cancer detection rates
 - 17% reduction in FP



Screening whole breast US (SWBUS)

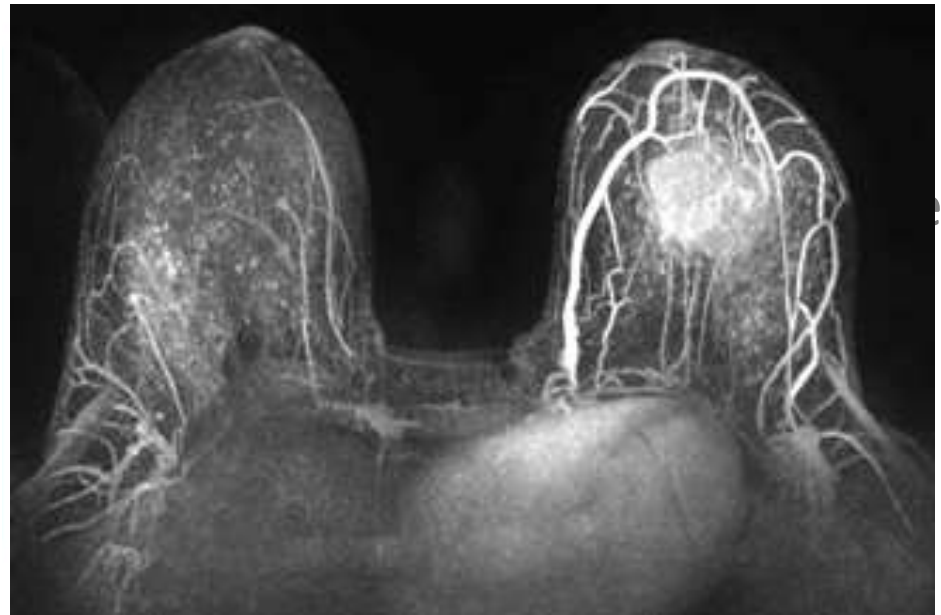
- Screening US evaluated in several prospective trials
 - USA ACRIN 6666 trial for high risk women¹ (n=2809)
 - Italian ASTOUND trials for dense breasts² (n=5300)
- Higher incremental CDR (4-5 per 1000 screens) but also higher rates of FP (1%)
- Technician dependent, resource intensive



American Society of Breast Surgeons, breast360.org

Screening MRI

- Functional assessment of breast tissue, detects neovascularity and peritumoral inflammation via the use of IV contrast gadolinium
- Highest sensitivity, but higher false positives



- 2011 Task Force: Reduction in breast cancer mortality for women aged 40-74 years, but equivocal net benefit for those under 50
- 2018: Updated recommendations for women not at increased risk, defined as:
 - No personal or FHx of breast cancer
 - No personal or FHx of a BRCA1/2 gene mutation
 - No history of chest wall radiation (lymphoma)

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- **Screening women aged 40 to 49 years:** For women aged 40 to 49 years, we recommend not screening with mammography; the decision to undergo screening is conditional on the relative value a woman places on possible benefits and harms from screening (conditional recommendation; low-certainty evidence)
- **Screening women aged 50 to 69 years:** For women aged 50 to 69 years, we recommend screening with mammography every 2 to 3 years; the decision to undergo screening is conditional on the relative value that a woman places on possible benefits and harms from screening (conditional recommendation; very low-certainty evidence)
- **Screening women aged 70 to 74 years:** For women aged 70 to 74 years, we recommend screening with mammography every 2 to 3 years; the decision to undergo screening is conditional on the relative value that a woman places on possible benefits and harms from screening (conditional recommendation; very low-certainty evidence)

- We recommend not using magnetic resonance imaging, tomosynthesis or ultrasound to screen for breast cancer in women who are not at increased risk (strong recommendation; no evidence)
 - ⊗ Dense breasts – Tomosynthesis & US can be helpful
- We recommend not performing clinical breast examinations to screen for breast cancer (conditional recommendation; no evidence)
 - ⊗ Women not undergoing mammographic screening
- We recommend not advising women to practice breast self-examination to screen for breast cancer (conditional recommendation; low-certainty evidence)
 - ...but we still want you to come to us if you feel something is new and have 'breast familiarity'*

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- **Screening women aged 50 to 69 years:** For women aged 50 to 69 years, we recommend screening with mammography every 2 to 5 years; the decision to undergo screening is conditional on the relative value that a woman places on possible benefits and harms from screening (conditional recommendation; very low-certainty evidence)
- **Screening women aged 70 to 74 years:** For women aged 70 to 74 years, we recommend screening with mammography every 2 to 3 years; the decision to undergo screening is conditional on the relative value that a woman places on possible benefits and harms from screening (conditional recommendation; very low-certainty evidence)

What is the evidence for these age specific recommendations?

HISTORICAL TRIALS

MAMMOGRAPHIC SCREENING RCTs

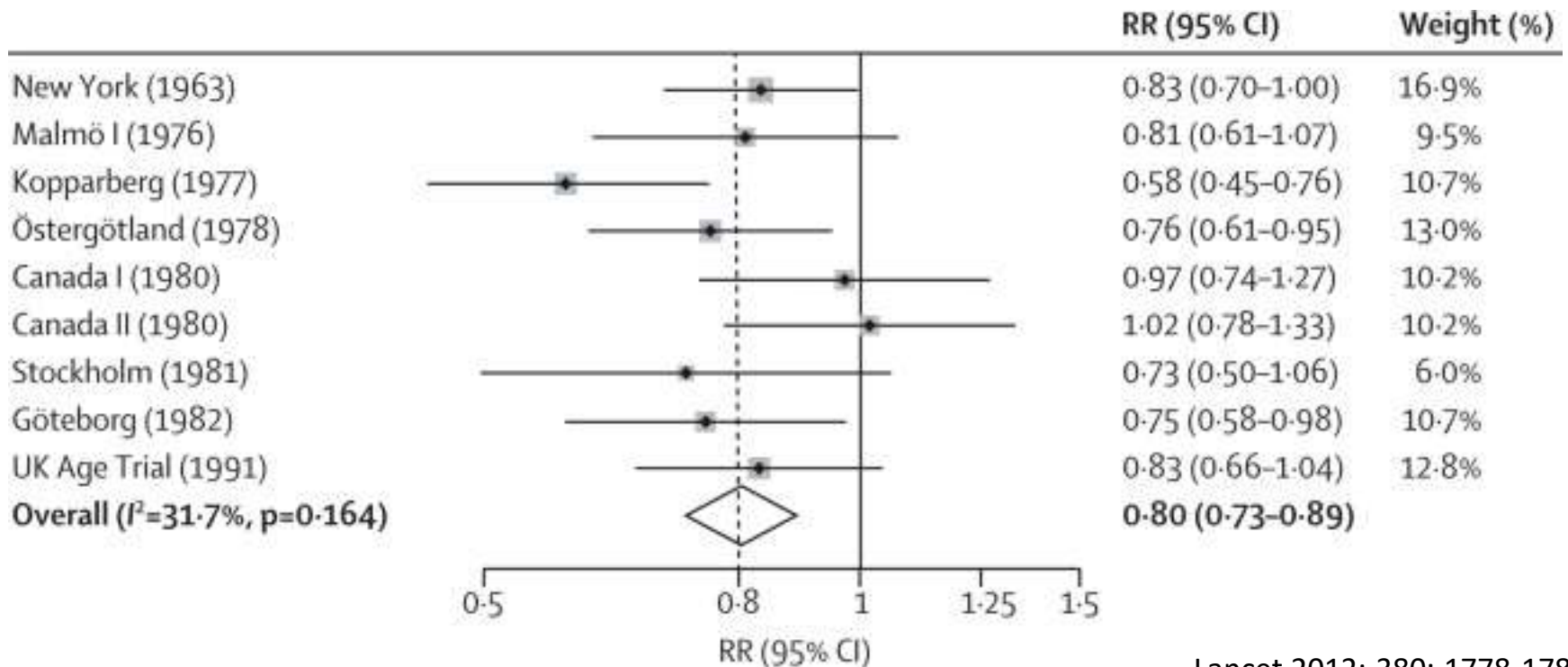
	No. Patients	Comparison Groups	Study Duration + Longest FU	Screening Characteristics
Canadian National Breast Screening Study (CNBSS-1, CNBSS-2) 1980 (40-49, 50-59)	50,430 (40-49 yrs), 39,405 (50-59 yrs)	Prescreened with CBE + BSE; Mammography + CBE vs. annual CBE	4 / 25 yrs	12 month intervals, 4 rounds, 85% adherence
Swedish Two County Trial 1977-78 (40-70)	77,080 (screened) 55,985 (control)	Mammography vs. usual care, controls offered screening after 7 years	7 / 20 yrs	24-33 month intervals, 3 rounds, 84% adherence
UK Age Trial 1991 (39-41)	53,884 (screened) 106 956 (control)	Mammography vs. usual care, all offered screening at age 50-52	9 / 17.5	12 month intervals, 4- 6 rounds, 57% adherence

+ others NY HIP (1963), Gothenberg trial (1982), Stockholm (1981), MMST 1 and MMST II (1976)

Relative risk reduction in breast cancer
mortality of 20%

MORTALITY BENEFIT





MAMMOGRAPHIC SCREENING RCTs



Lancet 2012; 380: 1778-1786

Relative risk reduction in breast cancer mortality of 20%

Table 1. Age-Specific Rates of Breast Cancer Mortality Reduction With Screening

Age	Mortality Rate in the Control Group per 100 000 Person-Years (95% CI)*	Breast Cancer Mortality Reduction: Relative Risk (95% CI)†	Deaths Prevented With Screening 10 000 Women Over 10 Years (95% CI)
Long case accrual			
39-49 y	36 (29 to 43)	 0.92 (0.75 to 1.02)	2.9 (-0.6 to 8.9)
50-59 y	54 (50 to 58)	 0.86 (0.68 to 0.97)	7.7 (1.6 to 17.2)
60-69 y	65 (52 to 81)	 0.67 (0.54 to 0.83)	21.3 (10.7 to 31.7)
70-74 y	62 (48 to 80)	 0.80 (0.51 to 1.28)	12.5 (-17.2 to 32.1)
50-69 y	58 (55 to 62)	0.78 (0.68 to 0.90)	12.5 (5.9 to 19.5)

Nelson et al. USPSTF Meta-analysis Update, Ann Intern Med 2016

39-49 yrs: No Mortality Benefit

50-59 yrs: 14% Mortality Reduction, 8 deaths prevented / 10,000 women

60-69 yrs: 33% Mortality Reduction, 21 deaths prevented / 10,000 women

70-74 yrs: 20% Mortality Reduction, 12.5 deaths prevented / 10,000 women

**= 4 deaths prevented / 1,000 women screened from
50-74 years**

Are these results still relevant?

All RCTs used outdated screening techniques, were subject to considerable bias, and do not take into account improvements in local and systemic therapies...

Pan-Canadian Study of Mammography Screening and Mortality from Breast Cancer

Andrew Coldman, Norm Phillips, Christine Wilson, Kathleen Decker, Anna M. Chiarelli, Jacques Brisson, Bin Zhang, Jennifer Payne, Gregory Doyle, Rukshanda Ahmad

- n=2,796,472 Canadian women, 1990-2009

Province	Program characteristics (19)		Population screening participation (19)	
	Program start year	Program recall by age, y† A = annual B = biennial	Participation in program among women aged 50–69 years in 2005–2006 (%)	Self-reported bilateral mammography among women aged 50–69 years in 2005–2006 (%)
BC	1988	B(50–79)‡ A(40–49)	51.1	60.1
MB	1995	B(50–69)	52.5	56.1
ON	1990	B(50–74)	32.4	62.7
QC	1998	B(50–69)	51.7	64.3
NB	1995	B(50–69)	53.0	62.8
NS	1991	B(50–69) A(40–49)	45.8	59.8
NL	1996	B(50–69)	35.4	61.5

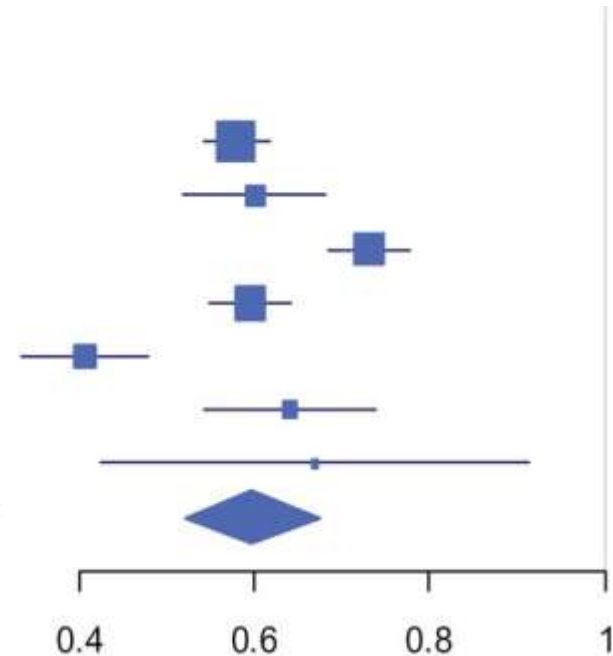
32-64%
participation rate
across provinces
(2006)

Cumulative incidence rates of breast cancer and five-year survival rates for screening program participants and nonparticipants aged 50 to 69 years by province*

Province	Cumulative incidence rate of invasive breast cancer between ages 50 and 69 years (%)		Breast cancer-specific five-year survival rate (%)	
	Participant	Nonparticipant	Participant	Nonparticipant
BC	7.2	5.2	94.4	85.1
MB	7.9	5.5	93.1	86.2
ON	6.9	5.4	93.1	85.6
QC	8.1	5.7	95.0	87.8
NB	7.0	5.3	95.8	83.2
NS	7.8	5.1	94.7	84.9
NL	7.9	5.1	94.0	85.5

* BC = British Columbia; MB = Manitoba; NB = New Brunswick; NL = Newfoundland and Labrador; NS = Nova Scotia; ON = Ontario; QC = Québec.

Region	SMR	95% CI
British Columbia	0.58	0.54 to 0.62
Manitoba	0.60	0.52 to 0.68
Ontario	0.73	0.68 to 0.78
Quebec	0.59	0.55 to 0.64
New Brunswick	0.41	0.33 to 0.48
Nova Scotia	0.64	0.54 to 0.74
Newfoundland and Labrador	0.67	0.42 to 0.91
Summary (random)	0.60	0.52 to 0.67



40% relative reduction in breast cancer mortality in real-world screened Canadian women relative to those who do not participate in screening

Table 3. Estimated Relative Reduction in Breast Cancer Mortality Associated With Mammography Screening, by Study Design Among Pooled Studies

Source	Study Design	Sample Size or Population	Age Range, y	Period or Duration of Follow-up, y	Exposure or Intervention	Relative Mortality Reduction With Screening (95% CI or Range)
Case-Control Studies						
Broeders et al ²⁹	Meta-analysis of 7 studies; publication years, 2004-2012	18 842	40->79	1987-2008	Screening mammography	OR, 0.46 (0.4-0.54)
					Screening mammography (corrected for self-selection)	OR, 0.52 (0.42-0.65)
					Invitation to screening mammography	OR, 0.69 (0.57-0.83)
Incidence-Based Mortality Studies						
Broeders et al ²⁹	Meta-analysis of 7 studies; publication years, 1997-2010	>2 million	45-69	6-22 y	Screening mammography	RR, 0.62 (0.56-0.69)
					Invitation to screening mammography	RR, 0.75 (0.69-0.81)
Randomized Clinical Trials						
Gøtzsche and Jørgenson, ³⁰	Meta-analysis of 7 trials; publication years, 1963-1991	289 552 invited, 309 538 not invited	39-74	7 and 13 y	Invitation to screening mammography	RR, 0.81 (0.74-0.87)
Model-Based Estimates						
Berry et al ⁴	7 models		30-79	NA	Screening mammography	Median, 15% (range, 7%-23%)

Abbreviations: NA, not applicable; OR, odds ratio; RR, relative risk.

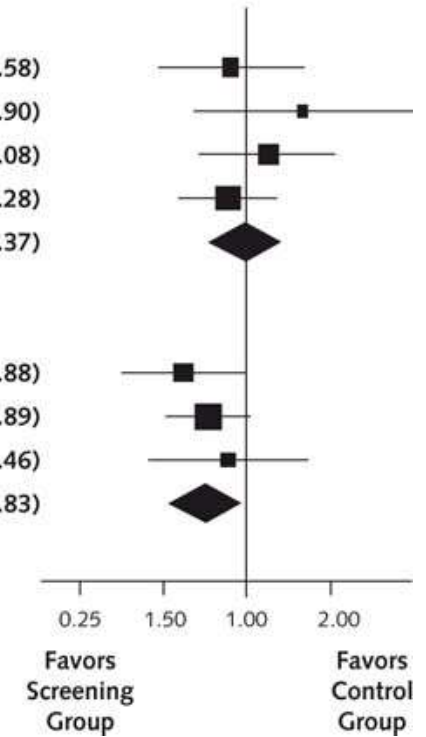
Why are mortality reductions greater in observational studies?

- Difference between participation and invitation
- Self-selection bias
- Improved treatment of early stage breast cancer
- Improvements in screening

EARLY DETECTION

LESS ADVANCED CANCERS

Author, Year (Reference)	Trial Name	Definition of Advanced Cancer	Events/Screening Group, n/N	Events/Control Group, n/N	Relative Risk (95% CI)
Women aged 39–49 y					
Chu et al, 1988 (68)	HIP	Stage III or greater	20/13 740	23/13 740	0.87 (0.48–1.58)
Tabár et al, 1995 (26)	Swedish Two-Country	Size ≥50 mm	14/19 844	7/15 604	1.57 (0.63–3.90)
Miller et al, 2002 (19)	CNBSS-1	Size ≥40 mm	26/25 214	22/25 216	1.18 (0.67–2.08)
Moss et al, 2005 (97)	Age	Size ≥50 mm	33/53 890	77/106 971	0.85 (0.57–1.28)
Overall ($I^2 = 0.0\%$; $P = 0.556$)			93/112 688	129/161 531	0.98 (0.74–1.37)
Women aged ≥50 y					
Chu et al, 1988 (68)	HIP	Stage III or greater	22/16 505	42/16 505	0.52 (0.31–0.88)
Tabár et al, 1995 (26)	Swedish Two-Country	Size ≥50 mm	62/57 236	69/40 381	0.63 (0.45–0.89)
Miller et al, 2000 (98)	CNBSS-2	Size ≥40 mm	15/19 711	20/19 694	0.75 (0.38–1.46)
Overall ($I^2 = 0.0\%$; $P = 0.692$)			99/93 452	131/76 580	0.62 (0.46–0.83)



Mortality...

“Old studies suggest that mammographic screening in women like you (without risk factors) reduces the risk of dying from breast cancer by 20%. But it is very important to remember that most women who get mammograms never develop breast cancer. It is also important to remember that because of medical advances in treatment, the majority of women diagnosed with breast cancer will never die from their breast cancer. So the number of lives saved from screening mammograms is actually very, very small.”

SHARED DECISION MAKING

BENEFITS AND HARMS

In 10,000 average risk women screened annually for 10 years...	From 40-50 years	From 50-60 years	From 60-70 years
No. diagnosed with invasive breast cancer	147	231	345
Breast cancer deaths	32	62	88
Deaths averted because of mammogram	3	10	43
One or more false positive	6130	6130	4970
At least one unnecessary biopsy	700	940	980
No. Overdiagnosed	28	44	66

Adapted from Keating NL et al. JAMA 2018



“If 100 average risk women undergo screening from 50-74, 6 will be diagnosed with breast cancer over the 25 year period, of whom, only 0.5% will have their lives saved because they underwent regular mammograms.”

Earlier stage of breast cancer...

“One of the benefits of mammograms is early detection. Evidence suggests that, for women over 50, screening mammograms can help detect cancers at an earlier stage, helping us to pick up smaller tumors that have not left the breast or spread to the lymph nodes. This can be an important factor for women because it may help them avoid certain treatments, namely chemotherapy. But some women who have their cancers picked up by mammograms may still require chemotherapy, even if identified early.”

There is a high likelihood of being called back at some point during their decades of screening for further imaging or a biopsy...

“Approximately 4% of women who undergo each screening mammogram get called back for further imaging; 80% of the time this is not cancer, and in the majority (70%) of cases, further imaging alone will help us know that there is nothing wrong. The remaining 30% of the time, a biopsy may be required to confirm that there is nothing wrong. The biopsy is done by a breast radiologist under image guidance. It usually takes 1-2 weeks for the results to come back, and if benign, this is what we consider a false positive biopsy.”

There is a risk of overtreatment...

“Long term, 1/5 to 1/10 women who undergo screening and have a diagnosis of breast cancer are overdiagnosed, meaning that they undergo treatment for a breast cancer that may have never produced symptoms or been apparent had they not been screened. Instead, they would have died from another causes without the breast cancer ever being a problem. Right now, of breast cancer patients, we do not know how to tell who these patients are.”

Patient Tool - Ages 50-59



Canadian Task Force
on Preventive Health Care

Breast Cancer Screening for Women Not at Increased Risk

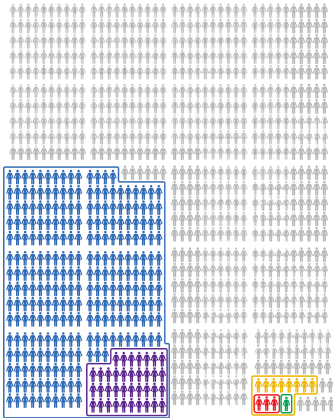


Updated Task Force Recommendations for Women

For women aged 50–59 years: we conditionally recommend *screening* for women not at increased risk with mammography every two to three years.

- The balance of benefits and harms is *more favourable* in this group.
- This recommendation is conditional because some women may wish to not be screened if they are concerned about potential harms.
- Women in this age group should have a discussion with their health care provider to decide if screening is the best option for them.

Screening 1000 women not at increased risk aged 50–59 over 7 years



With screening:

- 294 women will have a false positive test result
- 37 women will have an unnecessary biopsy
- 12 women will be diagnosed with breast cancer. Among these 12 women:
 - 3 will be treated for a breast cancer that would have never caused a problem
 - 1 breast cancer death will be prevented

1333 women in this age group would need to be screened to prevent one death

Who do these recommendations *not* apply to?

These recommendations don't apply to anyone at increased risk of breast cancer, such as those with a personal or family history of breast cancer, carriers of specific gene mutations (or who have a first-degree relative with these mutations), or chest radiation therapy before 30 years of age.

What is screening?

Screening is done to attempt to detect potential disease or illness in people who do not have any signs or symptoms of disease.

What is a mammogram?

It is an x-ray of the breast(s) to identify potential cancer.

Why is shared decision making important?

Screening is a personal decision. It is important to weigh the benefits and harms of screening for women in your age group (as shown below) with your health care provider to decide what is best for you.

What are the harms of screening for breast cancer?

Overdiagnosis - Not all breast cancers will cause harm to a woman in her lifetime. With screening, some women will be diagnosed with a cancer that would not have caused them a problem in their lifetime; this is called 'overdiagnosis' and leads to unnecessary treatment.

False positives - A false positive test occurs in someone who tested positive (abnormal mammography) but who ultimately is shown not to have cancer. It can lead to additional testing, including biopsy, and may cause psychological and physical harm.

In general, harms of screening are greater in younger women and decrease with age.

What are the benefits of screening for breast cancer?

There is evidence that shows that screening lowers a woman's risk of dying from breast cancer. In general, the benefits of screening increase with age.

This tool is not a decision aid but is intended to be one step in the shared decision making process.

Patient Tool - Ages 60-69



Canadian Task Force
on Preventive Health Care

Breast Cancer Screening for Women Not at Increased Risk

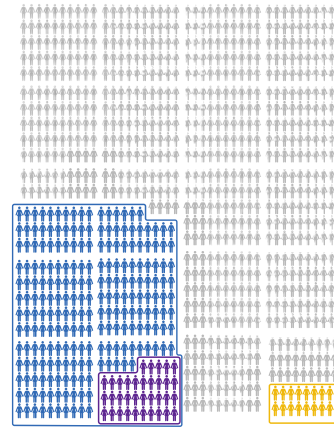


Updated Task Force Recommendations for Women

For women aged 60–69 years: we conditionally recommend *screening* for women not at increased risk with mammography every two to three years.

- The balance of benefits and harms is *more favourable* in this group.
- This recommendation is conditional because some women may wish to not be screened if they are concerned about potential harms.
- Women in this age group should have a discussion with their health care provider to decide if screening is the best option for them.

Screening 1000 women not at increased risk aged 60–69 over 7 years



With screening:

- 256 women will have a false positive test result
- 35 women will have an unnecessary biopsy
- 21 women will be diagnosed with breast cancer. Among these 21 women:
 - No reliable data on the number of women who were treated for a breast cancer that would have never caused a problem
 - 1 breast cancer death will be prevented

1087 women in this age group would need to be screened to prevent one death

Who do these recommendations *not* apply to?

These recommendations don't apply to anyone at increased risk of breast cancer, such as those with a personal or family history of breast cancer, carriers of specific gene mutations (or who have a first-degree relative with these mutations), or chest radiation therapy before 30 years of age.

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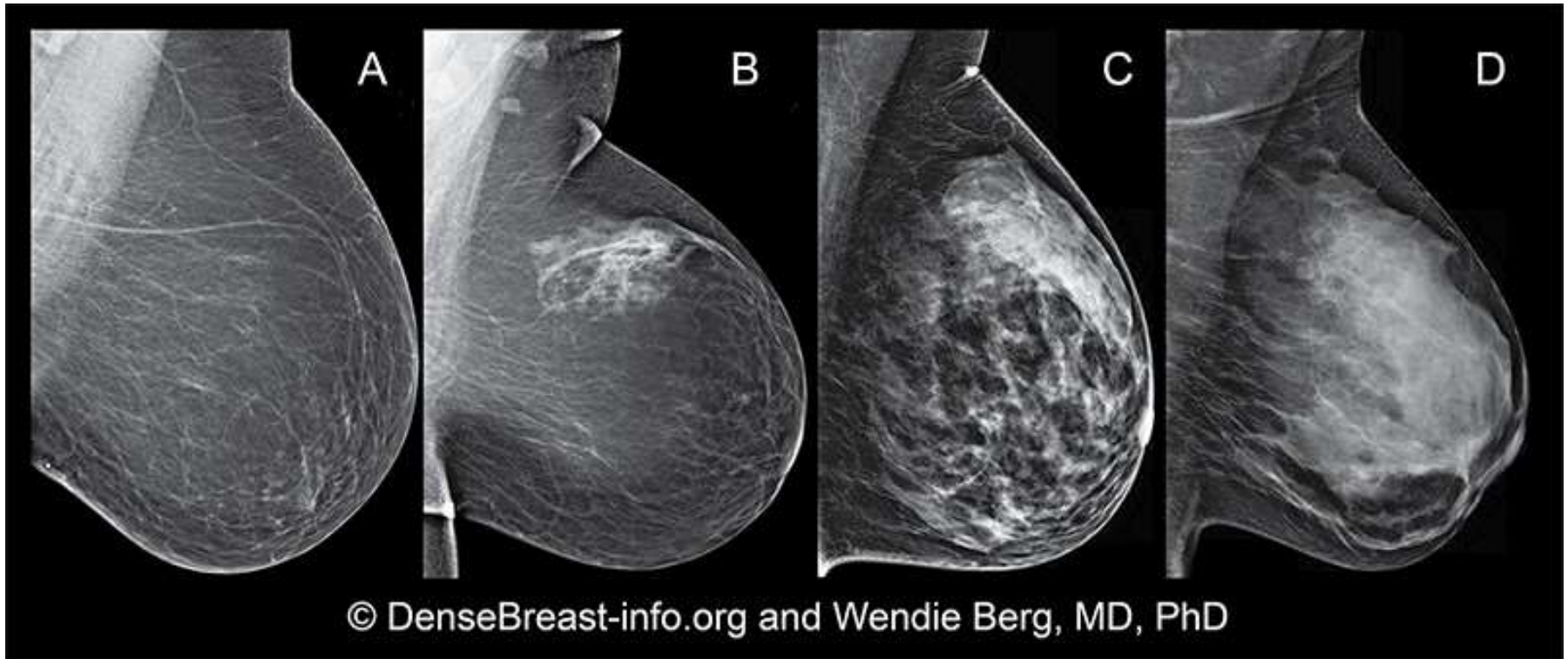
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DENSE BREASTS

ALTERS THE SENSITIVITY OF MAMMOGRAMS



Almost Entirely Fatty
(10%)

Scattered Fibroglandular
(40%)

Heterogeneously Dense
(40%)

Extremely Dense
(10%)

Not Dense: MG Sensitivity 80-98%¹

“Dense” Breasts: MG Sensitivity 30-48%¹

Ref

OR_{BreastCA}: 2.1 (1.6-2.6)²

OR_{BreastCA}: 2.4 (1.8-3.3)²

OR_{BreastCA}: 4.7 (3.0-7.4)²

¹Hooley RJ et al, Radiology 2012 ²Boyd et al, NEJM 2007 (Canadian Screening Programs)

Original Research

A prospective comparative trial of adjunct screening with tomosynthesis or ultrasound in women with mammography-negative dense breasts (ASTOUND-2)

Alberto S. Tagliafico ^{a,b,**}, Giovanna Mariscotti ^c, Francesca Valdora ^a,
Manuela Durando ^c, Jacopo Nori ^d, Daniele La Forgia ^e, Ilan Rosenberg ^f,
Francesca Caumo ^g, Nicoletta Gandolfo ^h, Maria Pia Sormani ⁱ,
Alessio Signori ⁱ, Massimo Calabrese ^j, Nehmat Houssami ^{k,*}

Multicentered trial
(4 centers in Italy)
Published EJC 2018
N=5300 women
Median age: 50 (43-79)

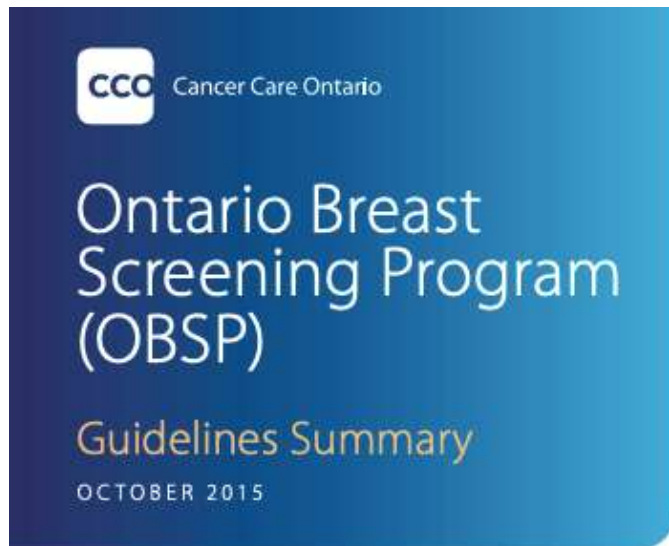
In 5300 women with negative mammograms + dense breasts...	Tomosynthesis	Ultrasound
Incremental Cancer Detection Rate (per 1000 screens)	2.83	4.90
False Positives	0.3%	1%
False Positives Requiring Biopsy	0.25%	0.93%

HIGH RISK PATIENTS

EARLIER INITIATION OF SCREENING

Risk Factor	Age of Initiation of Screening	Frequency of Screening
Dense Breasts	50 years	Annual Mammo +/- discuss DBT or US
Family history of onset breast cancer	10 years prior to youngest diagnosed family member or 50, whichever occurs first	Annual Mammo +/- DBT or US if dense
Atypical breast biopsy (ALH, ADH, LCIS)	40 years or at time of breast biopsy showing atypia	Annual Mammo +/- DBT or US if dense, consider MRI*
Moderate Penetrance Mutation Carrier (ATM, CHEK2, NBN, PALB2 without FHx)	10 years prior to youngest diagnosed family member, or starting at age 40, whichever occurs first*	Annual Mammo +/- DBT or US if dense, consider MRI*
High Penetrance Mutation Carrier (BRCA1/2, PTEN, CDH1, TP53, PALB2 with family history breast cancer)	25-30 years	Annual Mammo + Annual MRI (alternating every 6 months)
History of Chest Wall Radiation in Childhood	25-30 years	Annual Mammo + Annual MRI (alternating every 6 months)

*Insufficient evidence to support or refute/evidence in evolution



Screening Women at *High Risk for Breast Cancer*

Screen-eligible population

Women 30 to 69 years of age identified as high risk (see eligibility for criteria).

Screening recommendation

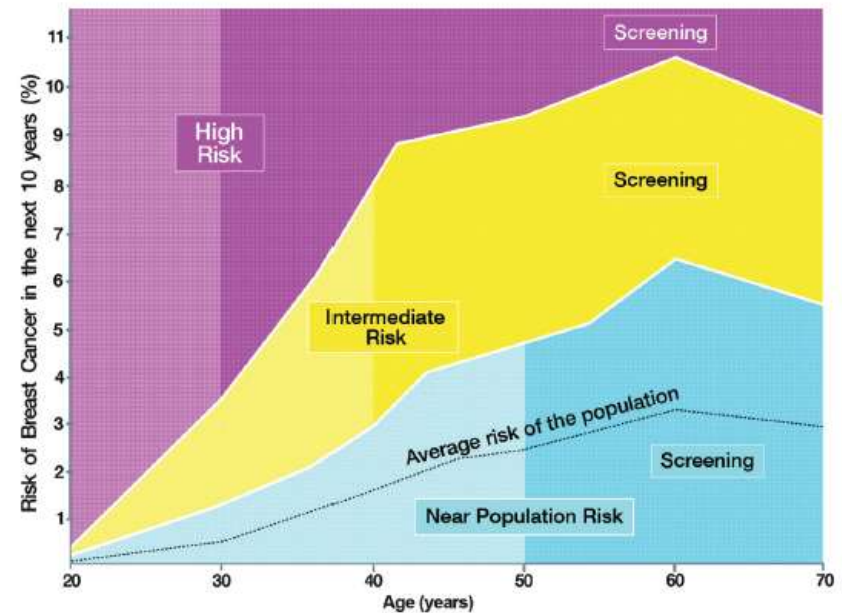
Screening mammogram and screening breast magnetic resonance imaging (MRI) every year (or, if appropriate, screening breast ultrasound) at OBSP high risk sites.

Eligible for direct entry into the high risk breast screening program based on personal and family history. Must meet one of the following risk criteria:

- Known to be a carrier of the BRCA1/2, PALB2, PTEN, CDH1, TP53 gene mutation;
- First-degree relative of a mutation carrier, has had genetic counselling and has declined genetic testing;
- Previously assessed by a genetic clinic (using the IBIS/Tyrer-Cuzick or BOADICEA tools) as having a ≥ 25 per cent personal lifetime risk of breast cancer based on family history; or
- Received radiation therapy to the chest before age 30 and at least eight years ago.

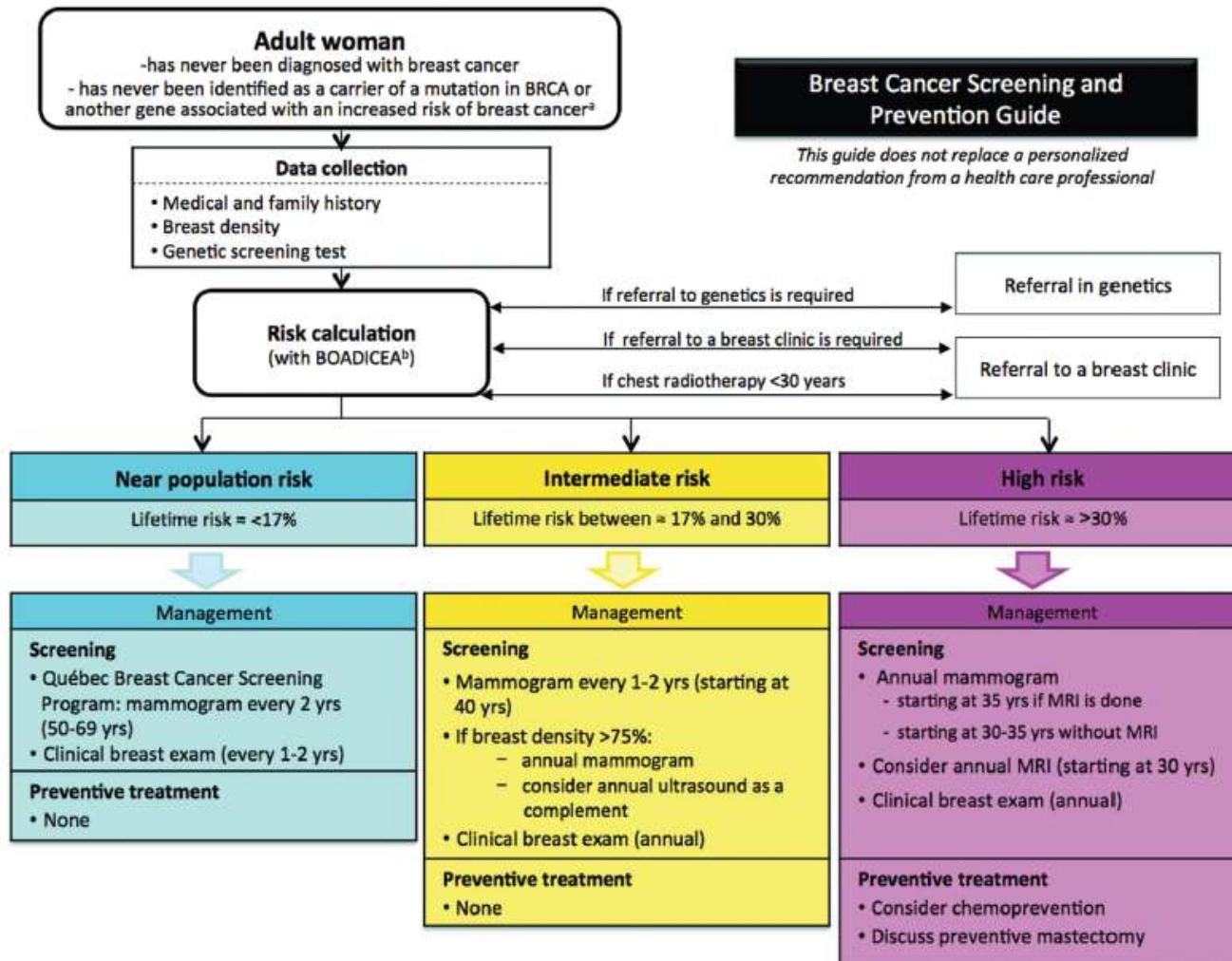
Quebec PERSPECTIVE (Personalized Risk Stratification for Prevention and Early Detection of Breast Cancer) Study

- Initiated in 2013, rolling out now
- Led by Jacques Simard (Laval) with \$15M grant funding from Genome Canada
- Risk assessment to facilitate establishment of screening schedules more in line with women's actual risk level
- Incorporates information on breast density, atypia, and genetic risk



HIGH RISK PATIENTS

PRE-EXISTING SCREENING PROGRAMS





HIGH RISK BREAST CLINIC

DESIGNED TO FOLLOW PATIENTS WITH...

ATYPICAL BREAST BIOPSIES

Lobular carcinoma in situ (LCIS), atypical lobular hyperplasia (ALH) & atypical ductal hyperplasia (ADH), and other atypias (flat epithelial atypia, atypical papillomas)

PERSONAL OR FAMILY HISTORY OF CANCER

Patients who have multiple close (1st or 2nd degree) relatives with breast cancer, a first degree relative with early onset breast cancer, any family history of ovarian cancer, or themselves have a history of cancer treated with chest wall radiation.

KNOWN GENETIC SUSCEPTIBILITY

Patients or families with known BRCA1/2 and PALB2 mutations, as well as women with other high penetrance (TP53, PTEN CDH1, STK11) or moderate penetrance mutations (ATM, CHEK2, NBN, etc.)

DENSE BREASTS

Women with extremely dense breasts (Category D) on screening mammography, tomosynthesis, or MRI.

OTHER RISK FACTORS

Women with actionable lifestyle risk factors such as obesity (BMI >40), smoking, and increased alcohol consumption (>7 drinks/week)



Hôpital général juif
Jewish General Hospital
Centre du cancer Segal Cancer Centre

BREAST CANCER SCREENING

Thank you!

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High Risk Breast Clinic (HRBC)
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Accepting Referrals via Fax To: (514) 340-8302
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