

Population Breast Cancer Screening in Canada

Applied Research in Cancer Control Conference

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Gregory Doyle

Chair, Canadian Breast Cancer Screening Network

Disclosure: Employed in cancer screening

Acknowledgments and thanks:

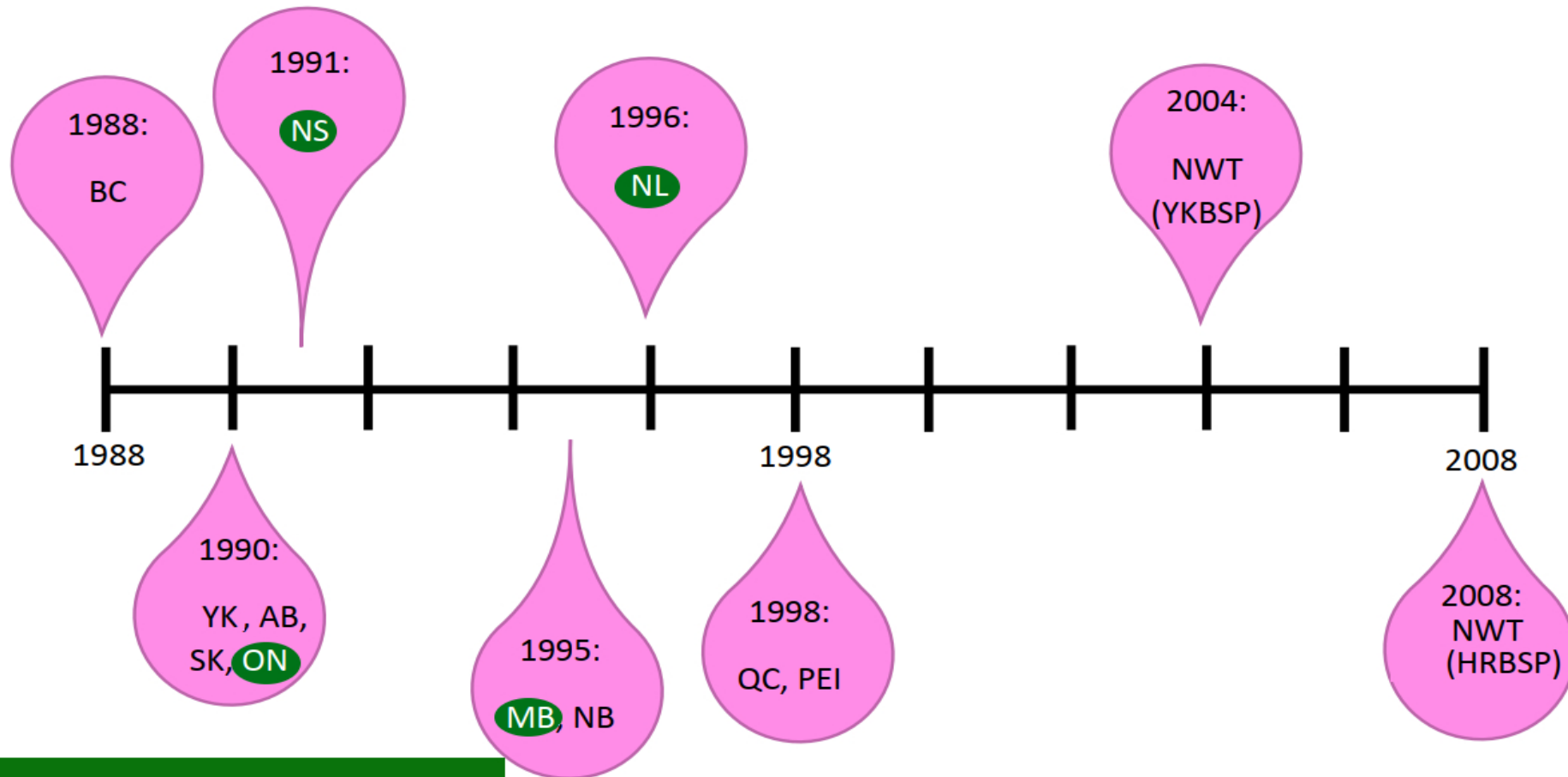
Canadian Partnership Against Cancer

- Screening and Early Detection Team
- System Performance Team

Outline:

- Who is screened for breast cancer
- Where and how screening for breast cancer occurs
- Why we started breast screening and why we do it today
- Screening outcomes in Canada

Program Implementation over 20 years



Screening ==> Mammography and Clinical Exam

Age and interval of Breast Screening in Canada

Province/Territory	Start Age		Default Interval	
	40 (self-referral)	40 <i>with PCP</i> Referral		50 (self-referral)
BC	✓		✓	Biennial
NS	✓		✓	Annual (40-49); Biennial (50+)
NWT, AB, NB		✓	✓	Biennial
YK, SK, MB, ON, PQ, PE, NL			✓	Biennial

Initial Invitation / Offer of Screening

Province/Territory	Initial Letter of Invitation to Screening (50-74)
AB, SK, MB, ON, PQ, NB	✓

Annual Screening – Elevated Risk

Province/Territory	Elevated Risk - Annual Screening		
	Family History	Breast Density $\geq 75\%$	Medical Hx - Benign Breast Disease
YK,	✓		
BC, PE	✓		✓
NWT, SK, ON, NS, NL	✓	✓	✓

Breast Screening Mammography – technology modality

Province/Territory	Analog	CR Mammo	FFDM	Tomosynthesis
ON	✓		✓	✓ (research setting)
BC			✓	✓ (research setting)
NB		✓	✓	✓
AB			✓	✓
PQ		✓	✓	
YK, NWT, SK, MB, PE, NS, NL			✓	

Why do we screen? - Taskforce Recommendations over the years....

1979

Condition and reference	Effectiveness of prevention and treatment	Quality of evidence	Maneuver
48. Cancer of the breast ¹⁹⁴⁻¹⁹⁷	Mortality in women aged 50 to 59 years is lowered by early detection through physical examination and mammography	I	For women aged 50 to 59 years: annual mammography and physical examination of the breast

1986

Since the publication of the 1979 report of the Canadian Task Force on the Periodic Health Examination,¹ the results of 5 more years of follow-up from the randomized controlled trial of breast cancer screening carried out by the Health

*Associate professor, Department of Health Care and Epidemiology, University of British Columbia, Vancouver

Insurance Plan (HIP) of Greater New York have become available.^{2,3} Surveillance now extends 16 years beyond the date of entry to the trial, and there are no significant changes in the conclusions to be drawn from the results of the study. Benefit continues to be maintained in the women who were 50 years or older when first screened, while the results remain equivocal for those under 50 at

Taskforce Recommendations over the years....

1994

Conclusions and Recommendations

Since all of the trials demonstrated a mortality reduction in the 50-69 age group, the Task Force recommends breast screening for women of this age (A Recommendation). Because the relative contributions of mammography and clinical examination have not yet been fully ascertained, both maneuvers are recommended. Also, since from the limited data available it is not possible to deduce confidently if biennial screening is as effective as annual screening, the Task Force advises that annual screening be maintained. Wherever possible, screening should be done at centers dedicated to this purpose.

In view of the absence of a significant benefit and the possibility that screening and intervention might be causing harm, the Task Force recommends that until further evidence is available, women age 40-49 not be screened (D Recommendation).

The evidence is not strong enough to make a clear recommendation on teaching breast self-examination; there is insufficient evidence to either include or exclude such teaching in periodic health examinations for women (C Recommendation).

1998 updated guidance for a screening interval of 1 to 2 years

Taskforce Recommendations over the years.... 2001

Table 6: Summary table of recommendation for screening mammography among women aged 40–49 years

Manoeuvre	Effectiveness	Level of evidence*	Recommendation*
Mammography every 12–18 months†	Relative risk reduction of 18%–45% for breast cancer mortality at 10 years was shown in 2 trials and 1 meta-analysis; no benefit was shown in 6 other trials‡	RCTs ^{2,3,5,6,15–42} (I)§	Current evidence does not support the recommendation that screening mammography be included in or excluded from the periodic health examination of women aged 40–49 at average risk of breast cancer (grade C)¶

Note: RCT = randomized controlled trial.

*See Appendix 1 for definitions of the levels of evidence and grades of recommendations.

†Comparison of RCT results suggests that, if done, frequent screening may be required. The value of adding clinical breast examination to mammography is unclear.

‡The only trial that enrolled Canadian women failed to show an effect of screening mammography, possibly because of low power.

§Six of the 7 RCTs assessed mammography for this age group as a subgroup analysis.

¶This represents a change from the 1994 grade D recommendation.⁴ Level I evidence is available, but some results conflict and not all relevant issues are resolved. Upon reaching the age of 40, Canadian women should be informed of the potential benefits and risks of screening mammography and assisted in deciding at what age they wish to initiate it.

Taskforce Recommendations over the years....

2001 - BSE

Recommendations:

- *Women aged 40–49 years:* Because there is fair evidence of no benefit, and good evidence of harm, there is fair evidence to recommend that routine teaching of BSE be excluded from the periodic health examination of women in this age group (grade D recommendation).
- *Women aged 50–69 years:* Because there is fair evidence of no benefit, and good evidence of harm, there is fair evidence to recommend that routine teaching of BSE be excluded from the periodic health examination of women in this age group (grade D recommendation).
- The lack of sufficient evidence to evaluate the effectiveness of the manoeuvre in women younger than 40 years and those 70 years and older precludes making recommendations for teaching BSE to women in these age groups. The follow-

Taskforce Recommendations over the years....

2011

Mammography

- For women aged **40–49 years**, we recommend **not routinely screening with mammography**. (*Weak recommendation; moderate-quality evidence*)
- For women aged **50–69 years**, we recommend **routinely screening with mammography every two to three years**. (*Weak recommendation; moderate-quality evidence*)
- For women aged **70–74 years**, we recommend **routinely screening with mammography every two to three years**. (*Weak recommendation; low-quality evidence*)

Clinical breast examination

- We recommend **not routinely performing clinical breast examinations alone or in conjunction with mammography** to screen for breast cancer. (*Weak recommendation; low-quality evidence*)

Breast self-examination

- We recommend **not advising women to routinely practice breast self-examination**. (*Weak recommendation; moderate-quality evidence*)

Taskforce Recommendations over the years....

2018

Mammography

- **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*).

World Health Organization Recommendations - 2014

1. Women aged 50–69 years

1.1 Well-resourced settings

In well-resourced settings, WHO recommends¹ organized, population-based mammography screening programmes for women aged 50–69 years if the conditions for implementing an organized programme specified in this guide are met by the health-care system, and if shared decision-making strategies are implemented so that women's decisions are consistent with their values and preferences. **(Strong recommendation based on moderate quality evidence)**

WHO suggests a screening interval of two years. **(Conditional recommendation based on low quality evidence)**

World Health Organization Recommendations - 2014

2. Women aged 40–49 years

3. Women aged 70–75 years

2.1 Well-resourced settings






In well-resourced settings, WHO suggests an organized, population-based screening programme for women aged 40–49 years only if such programme is conducted in the context of rigorous research, and monitoring and evaluation, if the conditions for implementing an organized programme specified in this guide are met by the health-care system, and if shared decision-making strategies are implemented so that women's decisions are consistent with their values and preferences. **(Conditional recommendation based on moderate quality evidence)**



EUROPEAN COMMISSION INITIATIVE ON BREAST CANCER

Breast Cancer Screening Recommendations -2016


Recommendation strength


-  *Strong recommendation against the intervention*
-  *Conditional recommendation against the intervention* **40 to 44,**
-  *Conditional recommendation for either the intervention or the comparison*
-  *Conditional recommendation for the intervention* **45 to 49, 70 to 74,**
-  *Strong recommendation for the intervention* **50 to 69,**

Recommendations based on 8 RCTS's 28 to 58 years since start of trials

Trial	Date	# of participants and ages	views	Frequency and # of rounds of screening	Follow –up	Results
HIP	1963	65,000	ML and CC and CBE	12 months	18 years	25% NSS 40-49
		40 - 64		4 rounds		25% SS 50-59
Malmo	1976	42,000	MLO and CC	18-24 months	8.8 years	20% SS
		>45	Or MLO only	5 rounds		
Swedish 2-C	1977	133,065	MLO only	40-49 24 months	30 years	30% SS 50-74
		40 - 74		50-74 33 months		30% non SS 40-49
				5 rounds		
Stockholm screening trial	1981	40,000 plus	MLO only	24 months	11 years	Borderline significant, 23%
		40 - 64		2 rounds only		
Gothenburg Trial	1982	30,000	MLO and CC	18 months	24 years	30% SS
		39 - 59	Or MLO only	5 rounds		
National Health Service – UK “Age” Trial	1991	160,921	MLO and CC	12 months	17.7 years	17% non SS
		39 - 47	Or MLO only	9 rounds		70% of invitees actually attended
						24% SS for attendees
CNBSS	1980	50,000	CC, MLO	12 months	21.9 years	Breast cancer deaths equal in both groups
		40 - 49		4 or 5 rounds		
		40,000				
		50 - 59				


Breast Screening in Canada – network activities

 Public Health Agency of Canada / Agence de la santé publique du Canada

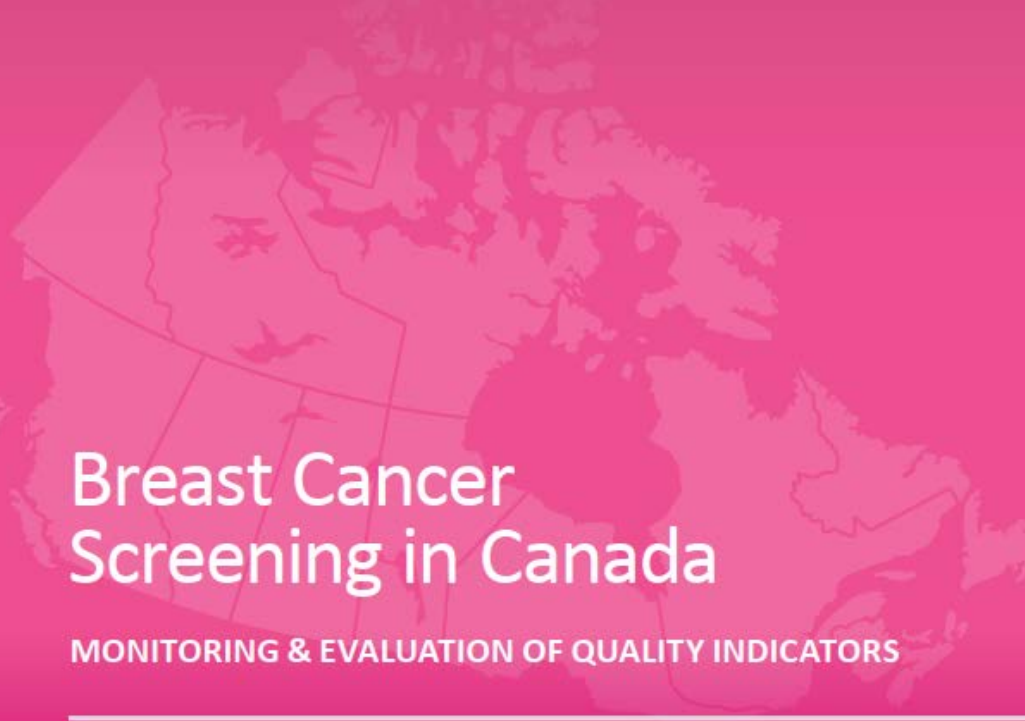


Information on Mammography

for Women Aged 40 and Older:
A Decision Aid for Breast Cancer Screening in Canada



Canada





Breast Cancer Screening in Canada

MONITORING & EVALUATION OF QUALITY INDICATORS

SPECIAL TOPIC:
Spotlight on Benefits and Harms

RESULTS REPORT
JANUARY 2011 – DECEMBER 2012

 CANADIAN PARTNERSHIP AGAINST CANCER /  PARTENARIAT CANADIEN CONTRE LE CANCER

Breast Screening: Quality Determinants and Evaluation Indicators

Quality Determinants of Breast Cancer Screening with Mammography in Canada

JANUARY 2013



Report from the Evaluation Indicators Working Group

GUIDELINES FOR MONITORING BREAST CANCER SCREENING PROGRAM PERFORMANCE

THIRD EDITION

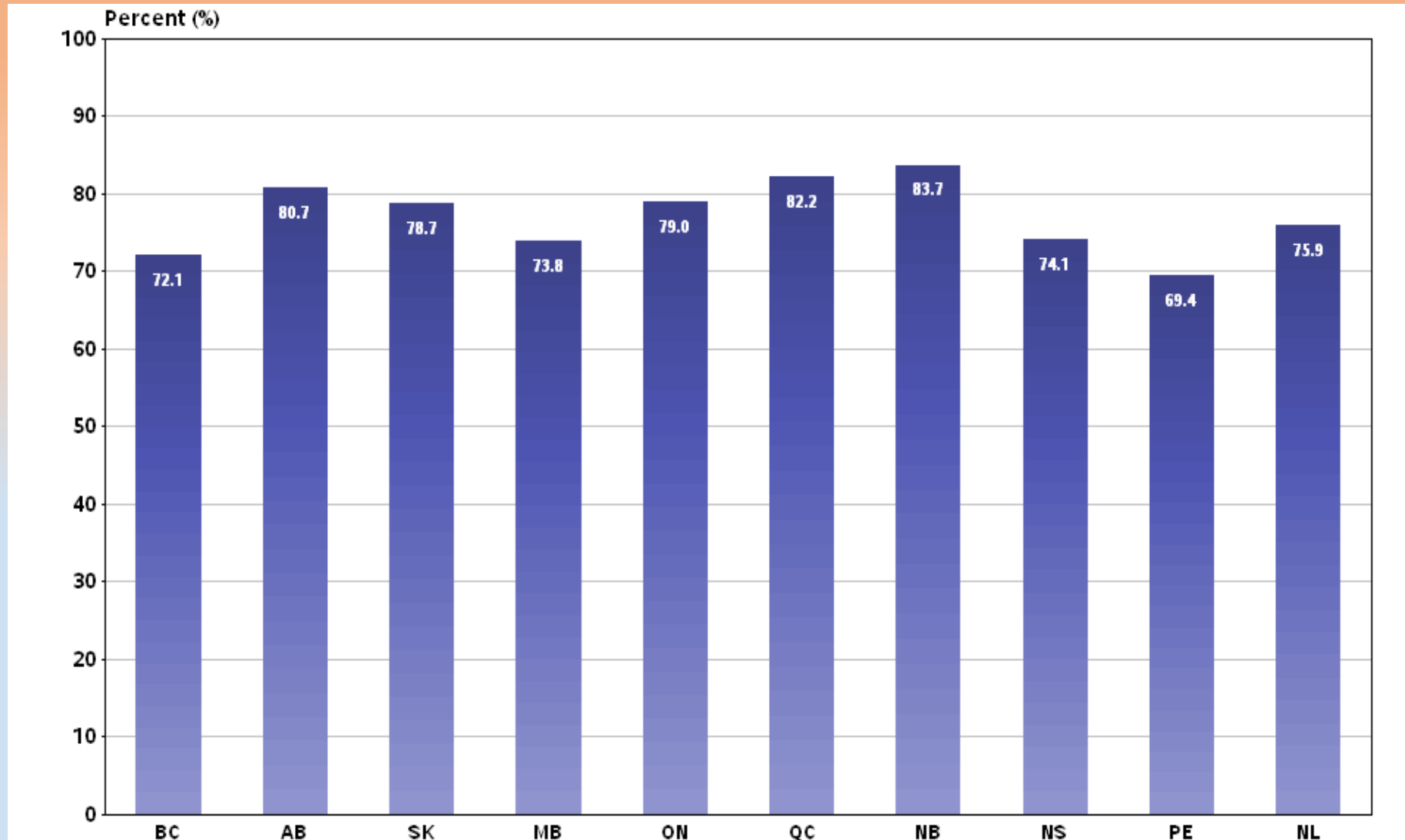


Breast Screening Evaluation Indicators

Evaluation Indicators for Organized Breast Cancer Screening Programs in Canada, Women Aged 50-69

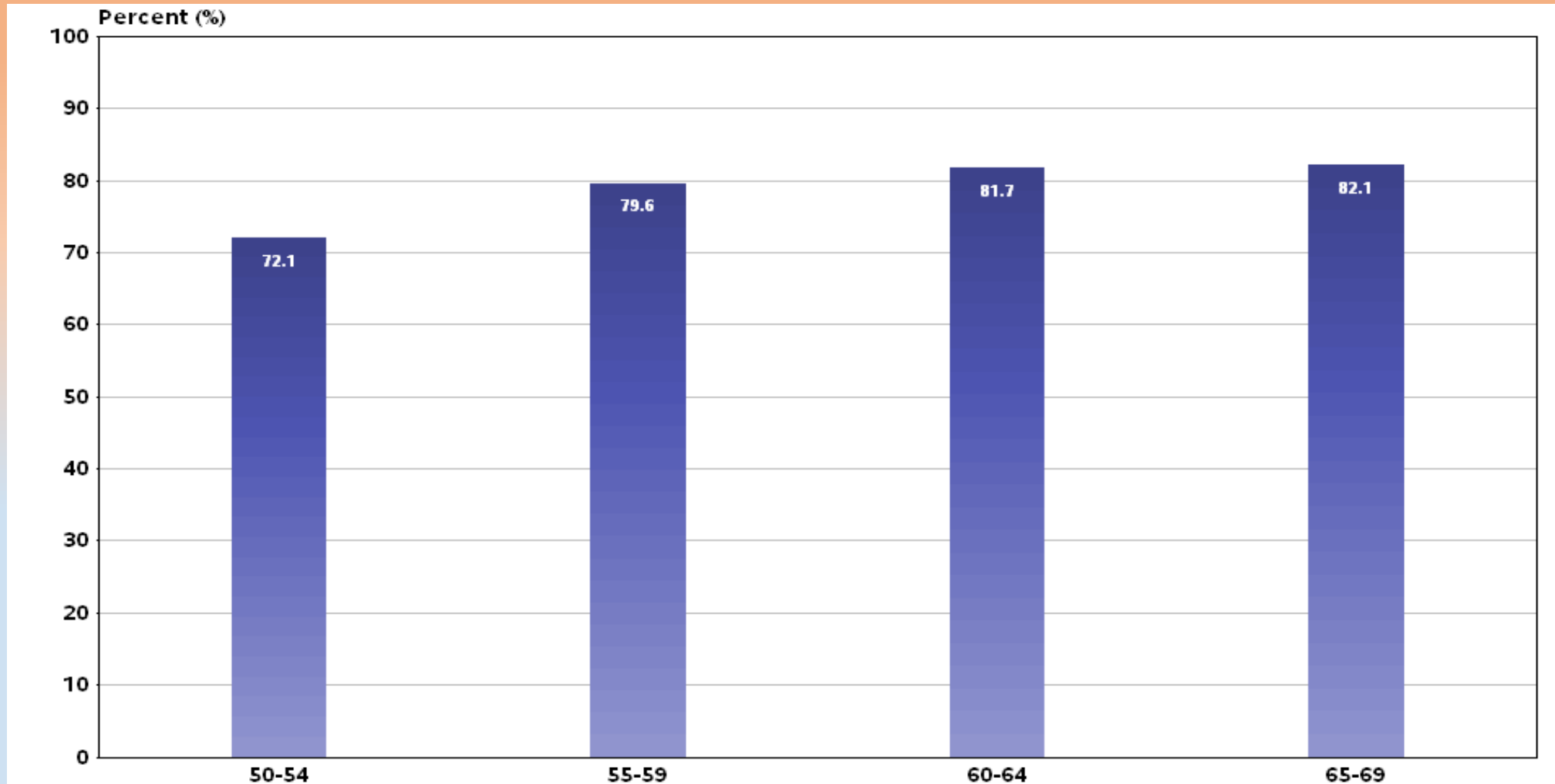
Indicator	Definition	Target
1. Participation rate	Percentage of women who have a screening mammogram (within a 30-month period) as a proportion of the target population.	≥ 70% of the target population within a 30-month period.
2. Retention rate	The estimated percentage of women age 50-67 who returned for screening within 30 months.	≥ 75% screened within 30 months of an initial screen; ≥ 90% screened within 30 months of a subsequent screen.
3. Annual Screening Rate	The estimated percentage of women aged 50-68 who are screened within 18 months of their previous screen.	% women screened within 18 months of an initial screen; % women screened within 18 months of a subsequent screen. (Surveillance and monitoring purposes only)
4. Abnormal call rate ^a	Percentage of mammograms that are identified as abnormal at program screen.	< 10% (initial screen); < 5% (subsequent screens).
5. Invasive cancer detection rate ^b	Number of invasive cancers detected per 1,000 screens.	> 5 per 1,000 (initial screen); > 3 per 1,000 (subsequent screens).
6. <i>In situ</i> cancer detection ^b	(a) Number of ductal carcinoma in situ (DCIS) cancers detected per 1,000 screens. (b) Percentage of all cancers that are DCIS.	(a) per 1,000 screens (initial); per 1,000 screens (subsequent screen). (Surveillance and monitoring purposes only). (b) % DCIS (initial); % DCIS (subsequent screen). (Surveillance and monitoring purposes only).

Percentage of women (aged 50-69) who had at least one mammogram in the past 3 years, by province (CCHS 2017)



Data source: Statistics Canada, Canadian Community Health Survey.

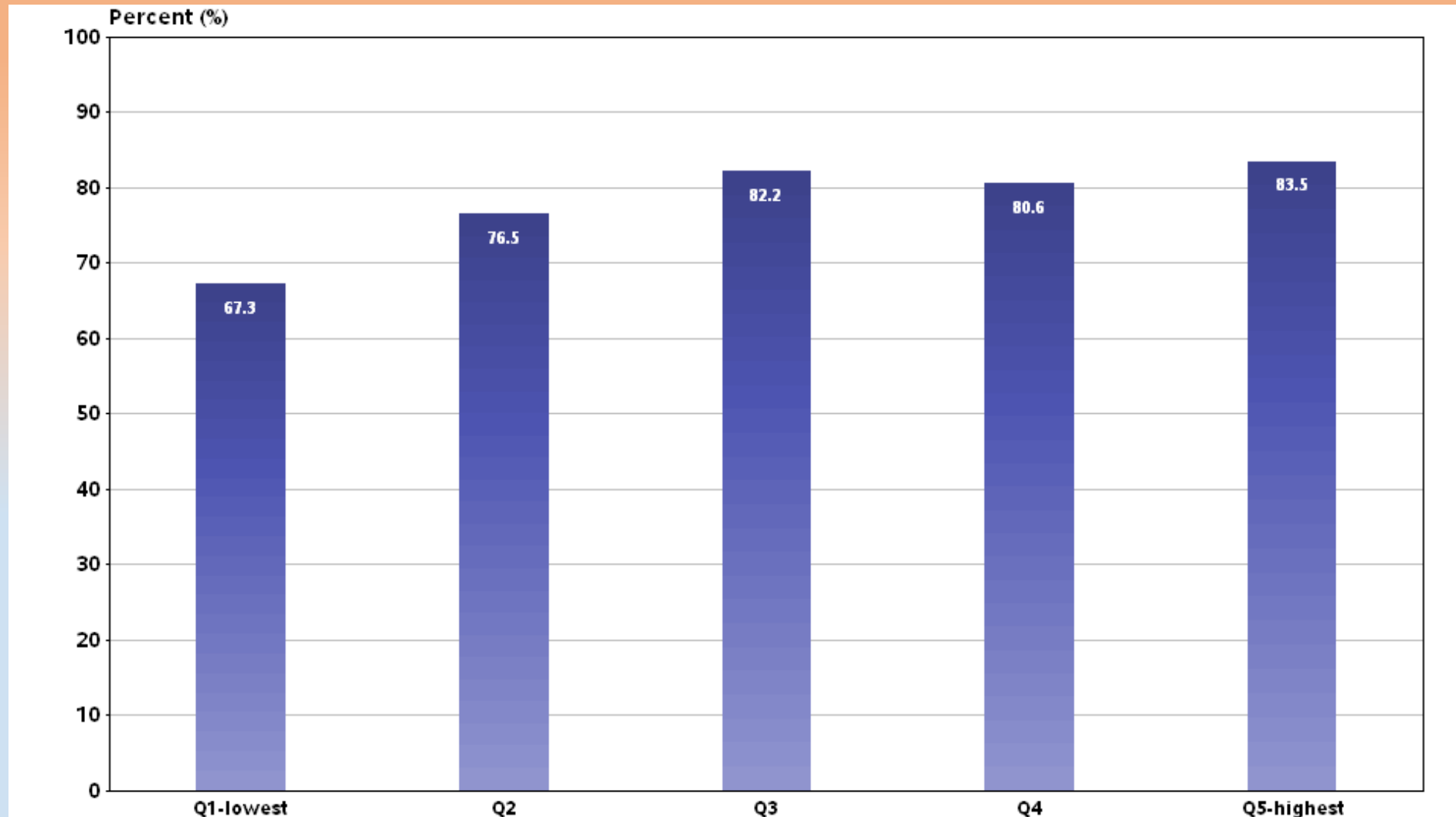
Percentage of women (aged 50-69) who had at least one mammogram in the past 3 years, by province (CCHS 2017)



†: include all 10 provinces.

Data source: Statistics Canada, Canadian Community Health Survey.

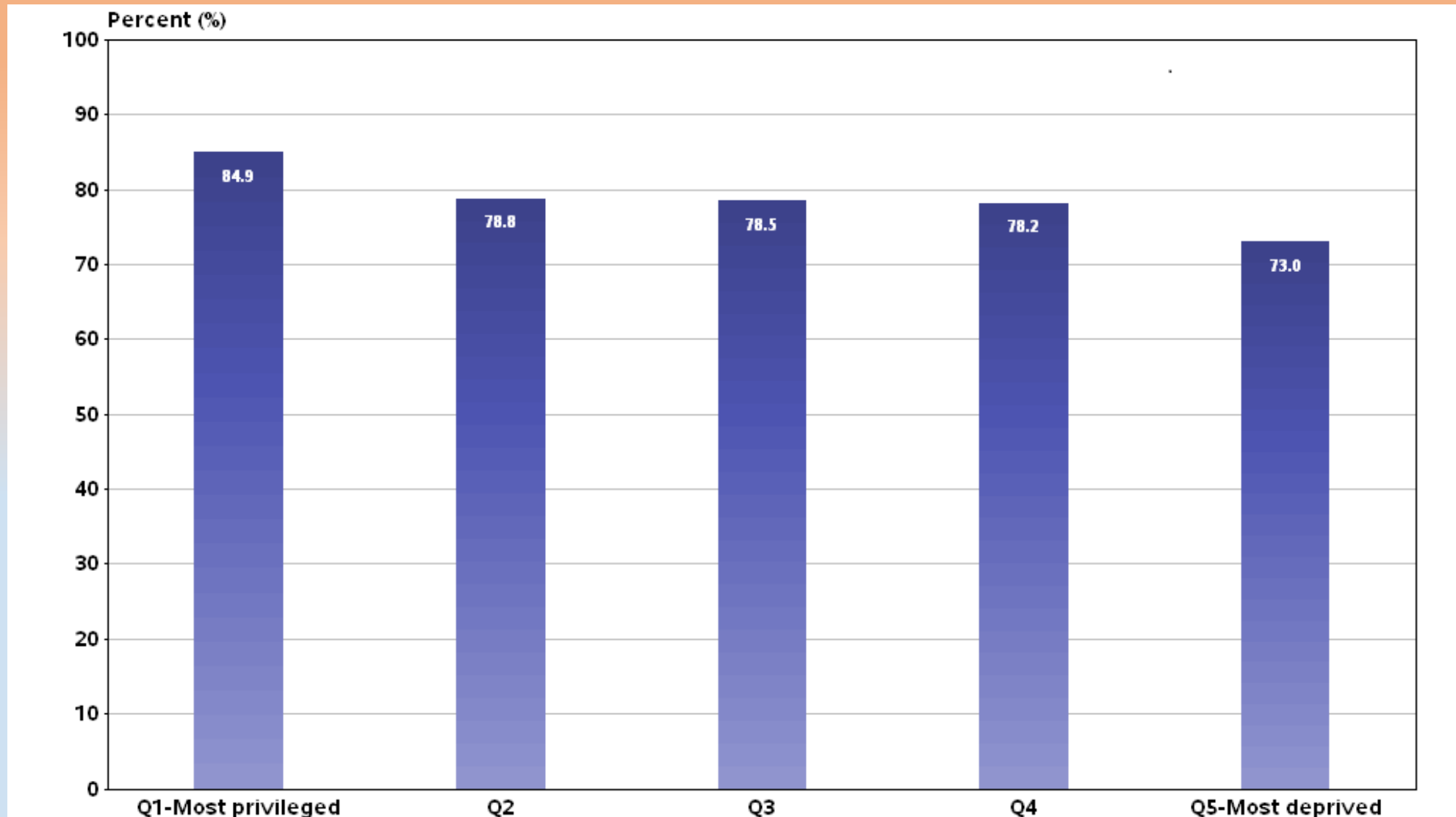
Percentage of women (aged 50-69) who had at least one mammogram in the past 3 years, by household income quintile, Canada[†] (CCHS 2017)



[†]: include all 10 provinces.

Data source: Statistics Canada, Canadian Community Health Survey.

Percentages of women (aged 50-69) who had at least one mammogram in the past 3 years, by social & material deprivation, Canada† (CCHS 2017)

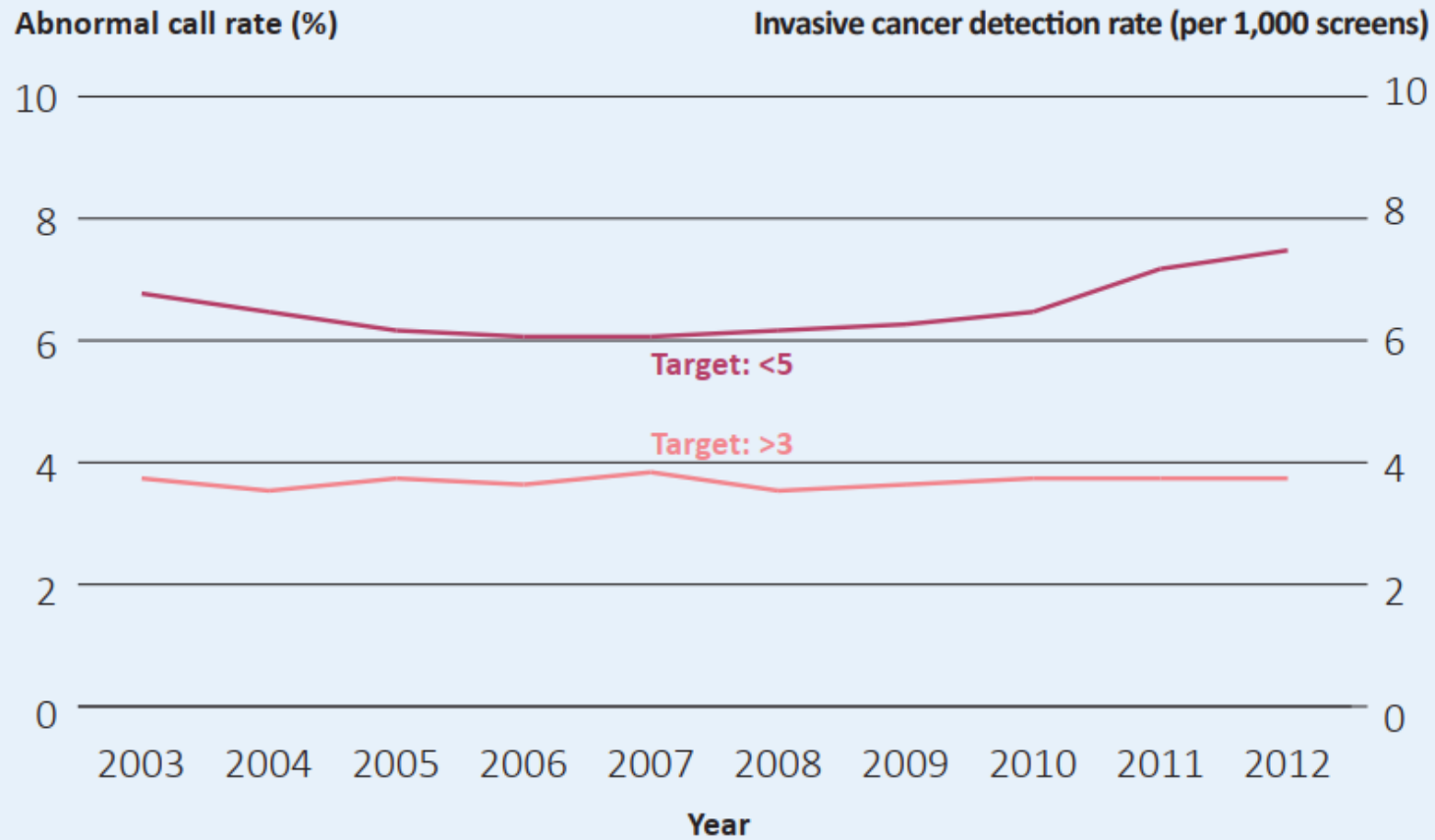


†: include all 10 provinces.

Data source: Statistics Canada, Canadian Community Health Survey.

Screening Outcomes: Abnormal call rates over nine years

Abnormal call rate and invasive cancer detection rate for subsequent screens,[†] women aged 50 to 69 years — from 2003 to 2012 screening years



■ Abnormal call rate, subsequent screen ■ Invasive cancer detection rate, subsequent screen

[†]Subsequent screens includes women who have been screened for breast cancer in the past, and excludes women new to the screening program. AB: Excluded from data prior to 2007 as the Alberta Breast Cancer Screening Program was launched in 2007. QC: Complete diagnostic/cancer information was available to September 30, 2012. Data source: Provincial and territorial breast cancer screening programs.

Impact of abnormal call rates on diagnostic investigations.

Current state
7.4%
Abnormal call rate
(2012)

➔

If reduced to
6.1%
Abnormal call rate
(2008)



21% of diagnostic investigations can be potentially avoided.

Canadian Partnership Against Cancer – Breast Screening Network

Halifax ACR Workshop – June 20, 2018

- Screening Programs
- Radiologists
- International Experts
- Review targets and trends
- Examine evidence and develop strategies to reduce the ACR

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

Manuscript received November 15, 2013; revised February 4, 2014; accepted July 17, 2014.

Correspondence to: Andrew Coldman, PhD, British Columbia Cancer Agency, #800 – 686W Broadway, Vancouver, BC V5Z 1G1, Canada (e-mail: acoldman@bccancer.bc.ca).

Background

Screening with mammography has been shown by randomized controlled trials to reduce breast cancer mortality in women aged 40 to 74 years. Estimates from observational studies following screening implementation in different countries have produced varied findings. We report findings for seven Canadian breast screening programs.

Methods

Canadian breast screening programs were invited to participate in a study aimed at comparing breast cancer mortality in participants and nonparticipants. Seven of 12 programs, representing 85% of the Canadian population, participated in the study. Data were obtained from the screening programs and corresponding cancer registries on screening mammograms and breast cancer diagnoses and deaths for the period between 1990 and 2009. Standardized mortality ratios were calculated comparing observed mortality in participants to that expected based upon nonparticipant rates. A substudy using data from British Columbia women aged 35 to 44 years was conducted to assess the potential effect of self-selection participation bias. All statistical tests were two-sided.

Results

Data were obtained on 2 796 472 screening participants. The average breast cancer mortality among participants was 40% (95% confidence interval [CI] = 33% to 48%), lower than expected with a range across provinces of 27% to 59%. Age at entry into screening did not greatly affect the magnitude of the average reduction in mortality, which varied between 35% and 44% overall. The substudy found no evidence that self-selection biased the reported mortality results, although the confidence intervals of this assessment were wide.

Conclusion

Participation in mammography screening programs in Canada was associated with substantially reduced breast cancer mortality.

Study:

- Comparison of breast cancer mortality among screening participants and nonparticipants
- Breast cancer mortality 40% lower among participants
- Participation in mammography screening associated with substantially reduced breast cancer mortality

Results:

- Mortality Reduction for ever-screened women (adjusted for age/ethnicity): 62%
- Further adjustment for selection bias – Mortality reduction (71% coverage): 34%
- Finding in agreement with other service screening evaluations and RCT's of mammography screening

Mammography service screening and breast cancer mortality in New Zealand: a National Cohort Study 1999–2011

Stephen Morrell¹, Richard Taylor^{*1}, David Roder², Bridget Robson³, Marli Gregory⁴ and Kirsty Craig⁴

¹School of Public Health and Community Medicine, University of NSW, Level 2, Samuels Building, Randwick, NSW, Australia; ²Sansom Institute for Health Research, University of South Australia, Adelaide, SA, Australia; ³University of Otago, Wellington, New Zealand and ⁴Breast Screen Aotearoa, National Screening Unit, Ministry of Health, Wellington, New Zealand

Background: This breast cancer mortality evaluation of service screening mammography in New Zealand, the first since commencement of screening in 1999, applies to the 1999–2011 diagnostic period. Individual-level linked information on mammography screening, breast cancer diagnosis and breast cancer mortality is used to analyse differences in breast cancer mortality according to participation in organised screening mammography, as provided by BreastScreen Aotearoa (BSA).

Methods: Women were followed from the time they became eligible for screening, from age 50 years (1999–2004) and 45 years (≥ 2004). Breast cancer mortality from cancers diagnosed during the screening period from 1999 to 2011 ($n = 4384$) is examined in relation to individual screening participation or non-participation during preceding person-years of follow-up from the time of screening eligibility. To account for changes from never- to ever-screened status, breast cancer mortality is calculated for each year in relation to prior accumulated time of participation and non-participation in screening. Breast cancer mortality is also examined in regularly screened women (screened ≥ 3 times and mean screening interval ≤ 30 months), and irregularly screened women compared with never-screened women. Statistical analyses are by negative binomial and Poisson regression with adjustment for age and ethnic group (Māori, Pacific women) in a repeated-measures analysis. Relative risks for breast cancer mortality compared with never-screened women, are adjusted also for screening selection bias, to indicate the extent of breast cancer mortality reduction in a population offered and not offered mammography screening. Prognostic indicators at diagnosis of breast cancer are also compared between different screening participation groups, including by grade of tumour, extent of disease (spread), multiple tumour status and maximum tumour size using χ^2 statistics, t-tests and two-sample median tests.

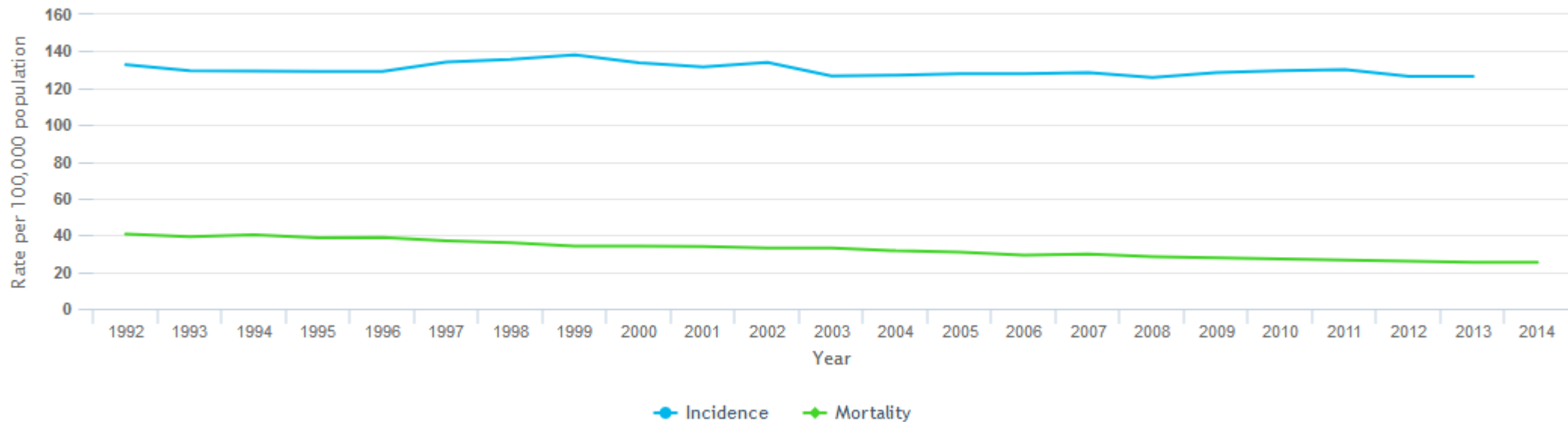
Results: For 1999–2011, after adjusting for age and ethnicity, breast cancer mortality in ever-screened women is estimated to be 62% (95% CI: 51–70) lower than in never-screened women. After further adjustment for screening selection bias, the mortality reduction in NZ is estimated to be 29% (95% CI: 20–38) at an average screening coverage of 64% for 2001–2011, and 34% (95% CI: 25–43) for recent screening coverage (2012–13, 71%). For irregularly screened women, the mortality reduction is estimated to be 31% (95% CI: 21–40), and 39% (95% CI: 22–52) in regularly screened women compared with never-screened women, after adjusting for age, ethnicity and screening selection bias (using recent 2012–2013 screening coverage of 71%). Ever-screened women diagnosed with breast cancer have more favourable prognostic indicators than never-screened women, with a higher proportion of localised cancer (63 compared with 46%), a higher proportion with a well-differentiated tumour (30 compared with 18%), lower risk of multiple tumours (RR = 0.48) and smaller median tumour size (15 mm compared with 20 mm)—all differences are statistically significant ($P < 0.0001$).

Conclusions: This is the first total population cohort study of an established nation-wide screening mammography programme using individual-level information on screening participation and mortality outcomes from breast cancer. The findings are in accord with other mammography screening service evaluations and with randomised trials of mammography screening.

Breast Cancer Incidence and Mortality Rates 1992 – 2014

- Incidence declined ~ 5%
- Mortality declined ~ 38%

Incidence and mortality rates[†] for breast cancer in women, Canada — from 1992 to 2014



[†] Age-standardized to 2011 Canadian population.

Data source: Statistics Canada, Canadian Cancer Registry (CANSIM), Vital Statistics Death Database.

Evidence on benefits of breast cancer screening (Barbeau et al, 2017)

- Eight RCTs or quasi-RCTs identified with information on benefits of breast cancer screening using mammography
 - Initiated from 1963 to 1991 in Sweden, Canada, US and UK.
 - Between 18,000 to 160,000 women were randomized in the trials with a mean follow-up from 18 to 30 years.
 - Screening intervals between 12 and 33 months.
 - Duration of the screening period was from 3 to 12 years (median 7 years).
 - Participation rates of 65% to 88%.
- **Certainty of the evidence from these trials assessed as being lower than in the review from 2011 due to very *serious* concerns around risk of bias.**



Certainty of the evidence...???

The RCT's
are
old...initiated
28 to 56
years ago

The technology
and quality of
Mammography
has vastly
improved

The body of knowledge and
expertise of radiology,
mammography accreditation,
population cancer screening,
medical physics, pathology,
and oncology have all
expanded exponentially. We
know so much more!

The RCT's bias is that they tell
us about the efficacy of
mammography film screening
circa 1985 and are not
informative of modern breast
cancer screening, early
detection, and breast imaging -
circa 2020

Thank you and Good Day!

The Argument against Mammography Screening

Anthony B. Miller, MD

Professor Emeritus, Dalla Lana School of
of Public Health, University of Toronto

ARCC 2019

The Expectation for Mammography Screening

- Early detection of breast cancer by mammography will reduce breast cancer mortality
- Such early detection will reduce the needed extent of treatment for breast cancer and reduce costs
- As mammography (and other forms of breast imaging) improve, the benefit will increase

We have to remember that case detection is not equivalent to benefit

- The detected cancer may not be curable, nor have its natural history modified by available treatment
- The detected cancer may never have become life-threatening in the patients lifetime because it is cured by treatment or overdiagnosed.

Randomized Trials of Mammography screening with and without clinical breast examination

Trial	Age at enrolment	No. of women	RR	95% CI
Health Insurance Plan, USA	40–65	60,995	0.78	0.61–1.00
Malmö I, Sweden	45–69	42,283	0.81	0.66–1.00
Malmö II, Sweden	45–57	17,793	0.65	0.39–1.08
Two–county, Sweden	40–74	133,065	0.73	0.59–0.89
Edinburgh, UK	45–64	44,268	0.70	0.62–0.97
Canada National, 1+ 2	40–59	89,835	1.05	0.85–1.30
Stockholm, Sweden	39–64	60,117	0.90	0.63–1.28
Göteborg, Sweden	39–59	51,611	0.79	0.58–1.08
Age trial, UK	39–41	160,921	0.83	0.66–1.04

Concerns over the Two-county trial

- Cluster randomisation, balance between the arms has never been confirmed
- Conducted in the pre-adjuvant chemotherapy era
- Only 3 single-view mammograms ~ 2 years apart
- Reduction in breast cancer mortality balanced by excess in non-breast cancer mortality

The issue of therapy

- No adjuvant therapy was used in the Two-county trial
- Adjuvant therapy freely available in the CNBSS

As therapy improves, the absolute benefit from screening will be reduced.

Conclusion on the Two-county trial

- The survival experienced by the women with breast cancer in the controls is not the current expectation, because of improved treatment.
- This has a major impact on the benefits derived from breast screening.
- The benefits from mammography screening as applied in the Two-county trial have been exaggerated.

CNBSS: Deaths from breast cancer

Cancers detected in:	Mammo-graphy arm	Control arm	Hazard ratio	95% Confidence intervals
Years 1-5	180	171	1.05	0.85-1.30
Years 1-25	500	505	0.99	0.88-1.12

CNBSS: Deaths from breast cancer by age

Cancers detected in years	Hazard ratio	95% Confidence intervals
1-5:		
Women age 40-49	1.09	0.80-1.49
Women age 50-59	1.02	0.77-1.36

CNBSS Study population – balance achieved by randomisation

	40-49		50-59	
	MA (n=25,214)	CO (n=25,171)	MA (n=19,711)	CO (n=19,694)
Married	80.6%	80.7%	79.0%	78.5%
Family history				
BC-First degree	11.4%	11.6%	14.1%	14.1%
Second degree	26.2%	26.7%	24.6%	24.4%
Premenopausal	66.4%	67.1%	13.5%	13.9%
Nulliparous	9.9%	10.1%	6.0%	6.3%
4 or more births	19.4%	20.0%	33.6%	33.4%
Never smoked	47.9%	47.7%	51.7%	52.1%
Not in workforce	33.1%	32.9%	46.0%	45.8%

CNBSS Referral to Review, first screen

Age	Mammography arm		Control arm	
	Number	%	Number	%
40-49	3569	14.1	3674	14.6
50-59	2164	11.0	2207	11.2

CNBSS-2 Invasive breast cancers detected in the screening period

Arm:	Mammography		Control
Palpable?	Yes	No	Yes
Tumour size	2.1 cm.	1.4 cm.	2.1 cm.
Lymph node			
Negative	252	142	303
Positive	169	35	170

Miscan Model estimates of effect of CBE in the CNBSS (Rijnsburger et al, 2004)

Breast cancer mortality reduction at 11 years in the PO arm of CNBSS 2 from annual CBE screening compared to no screening: 20.5% (19.7%-22.1%)

Conclusion on CNBSS

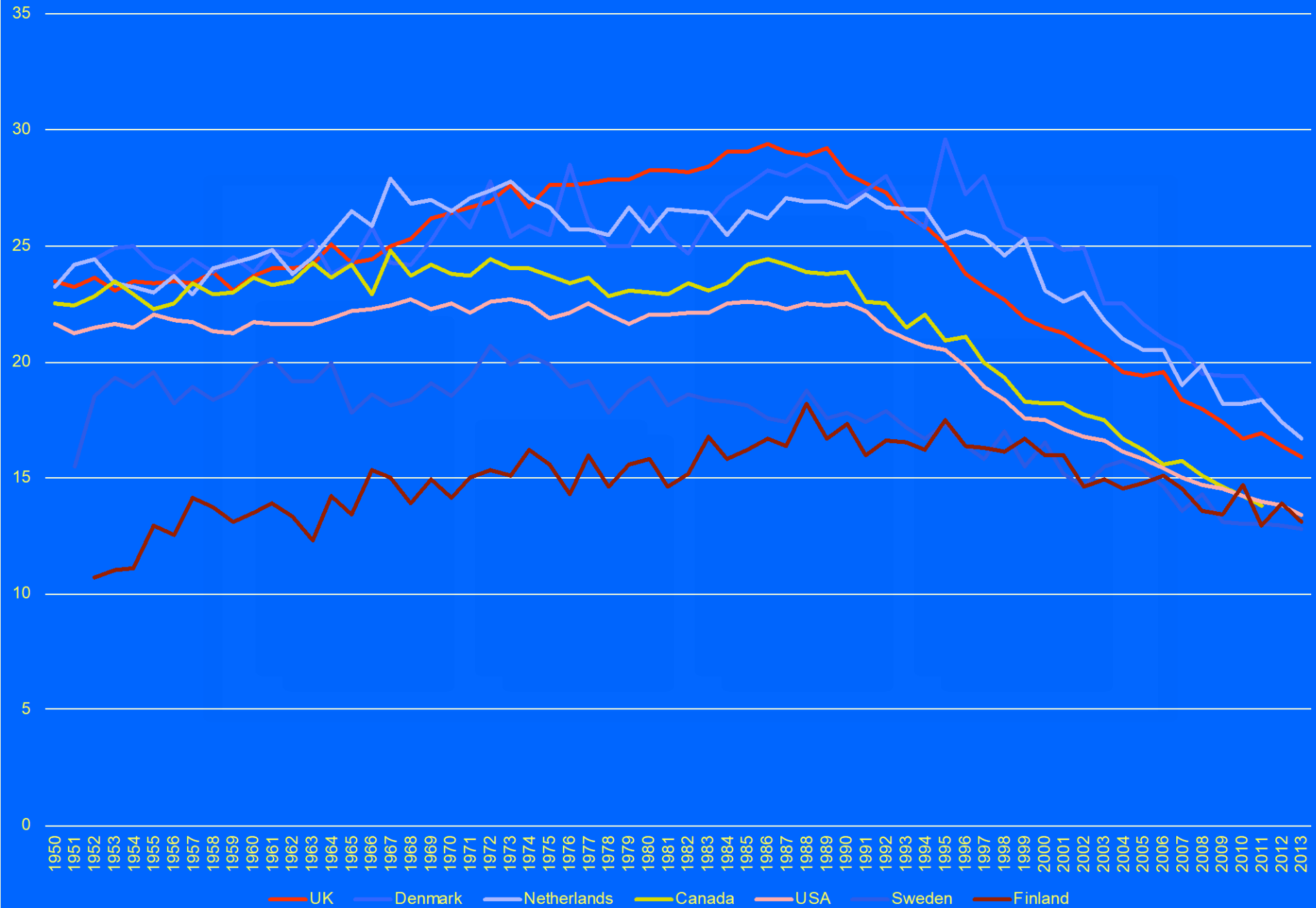
The benefit from screening derives from the earlier detection of advanced breast cancers, coupled with good therapy, not from the early detection of impalpable cancers.

This is accomplished both by good CBE and (perhaps) by mammography

Alternative Conclusion on CNBSS

There is no benefit from screening for breast cancer, whatever screening modality is used.

Trends in mortality from Breast Cancer



The Cisnet Models

(Berry et al, NEJM 2005; 353: 1784-92)

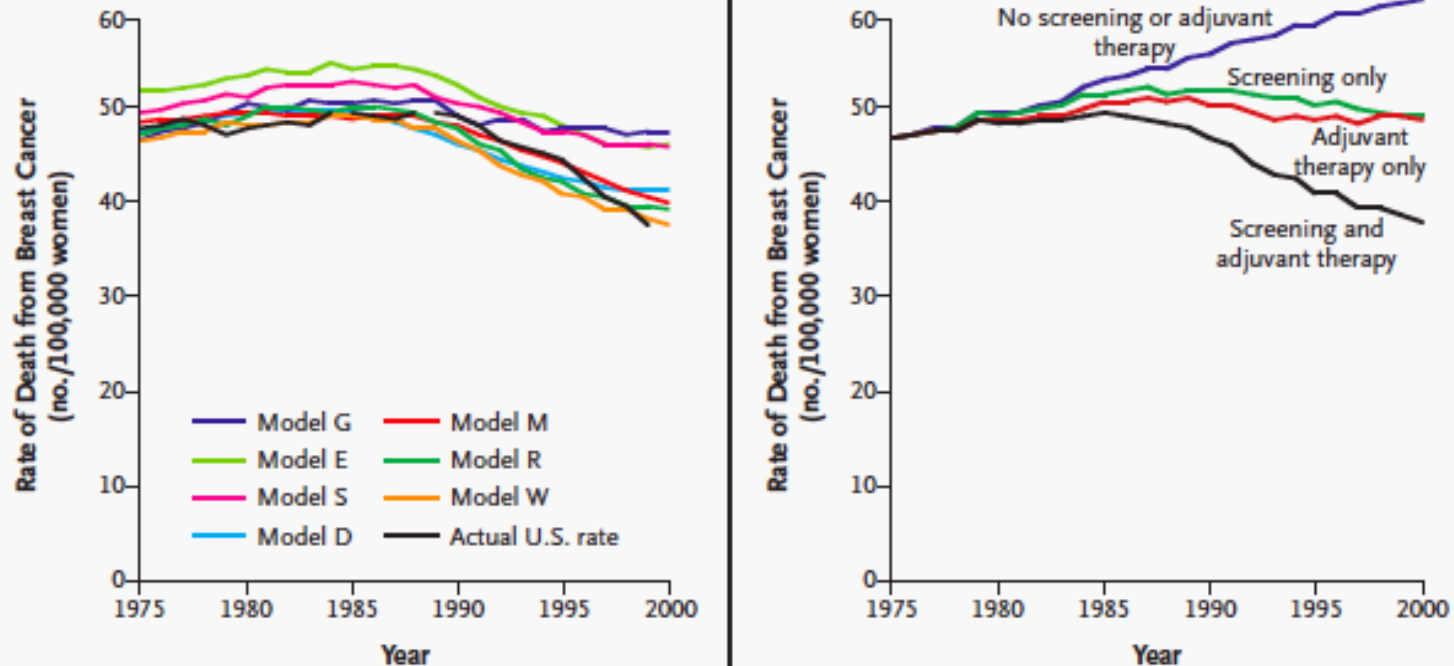


Figure 2. Estimated and Actual Rates of Death from Breast Cancer among Women 30 to 79 Years of Age from 1975 to 2000 (Panel A) and under Hypothetical Assumptions about the Use of Screening Mammography and Adjuvant Treatment (Panel B).

Panel A, which compares the model-based results with the actual rates in the United States from 1975 to 2000, shows the variability across the model estimates. Some of the models were calibrated according to the observed rate of death from breast cancer in the United States, and some were not. Panel B shows the results from model W (the University of Wisconsin–Madison) of estimated mortality trends for the four scenarios considered: no screening and no adjuvant treatment; base-case screening, but no adjuvant treatment; no screening, but base-case adjuvant treatment; base-case screening and adjuvant treatment. Rates in both panels are age-adjusted to the 2000 U.S. standard.

Incidence of breast cancer among women age 40 or more, United States (Bleyer and Welch, 2012)

	Before mammography (1976-1978)	Three decades later (2006-2008)
Early Stage Breast cancer:		
DCIS	7	56
Localized disease	105	178
Late Stage Breast cancer:		
Regional disease	85	78
Distant disease	17	17

Evaluation of Service Screening Programmes

Methodology used:

- Incidence based cohort studies, e.g. Coldman et al, 2014
- Case-control studies

The main problem:

- Inability to assemble a truly comparable comparison group, with identical treatment, thus bias and confounding can not be excluded – applies to both:
 - ◆ Screened versus unscreened
 - ◆ Geographic and historical comparisons

Overdiagnosis: Estimates from the Canadian National Breast Screening Study (Miller et al, 2014)

- Number of screen-detected invasive cancers: 484
- Numbers of overdiagnosed invasive cases: 106
- 22% screen-detected cases overdiagnosed
- 50% cases detected by mammography alone overdiagnosed

Overdiagnosis: Estimates from the Canadian National Breast Screening Study (Miller et al, 2014, To et al, 2014)

- Number of screen-detected invasive and *in situ* cancers: 589
- Numbers of overdiagnosed invasive and *in situ* cases: 206
- 35% screen-detected cases overdiagnosed
- 72% cases detected by mammography alone overdiagnosed

Implications of Overdiagnosis

- Overtreatment
- Our previous estimates of lead time were wrong, e.g. lead time gained by mammography is ~ 1 year, not 4 years
- We need research on biomarkers (molecular markers) to identify over-diagnosed cases

The Reality of Mammography Screening

- Early detection of breast cancer by mammography reduces breast cancer mortality by a vanishingly small amount
- Use of mammography for screening increases the needed extent of treatment for breast cancer and increases costs
- As mammography (and other forms of breast imaging) improve, the extent of overdiagnosis caused will increase

Conclusions

The meta-analyses and mathematical modelling conducted to date have over-estimated the benefit likely to be achieved by mammography screening in the era of adjuvant chemotherapy and hormone therapy

In many countries, mortality from breast cancer is falling, but the contribution of screening is small, the contribution of improved treatment is dominant

Breast Cancer Screening: what lies ahead?

Jennifer Payne, PhD

**Associate Professor
Dept of Diagnostic Radiology
Dalhousie University &
Senior Epidemiologist, NS Health Authority**

**ARCC Conference
Halifax, 31 Jan 2018**

Disclosures

- Financial:

- ▶ Spouse - Mohamed Abdolell, CEO, Densitas
- ▶ Salary - NS Breast Screening Program

- Perspective:

- ▶ Expert Reviewer, CTFPHC 2018 Breast Screening Guidelines
- ▶ Chair, Monitoring & Evaluation Working Group, Canadian Breast Cancer Screening Network, CPAC (2011-17)

Outline

- Evidence
- Outcome
- Risk

Evidence

Forms of Evidence



CTFPHC 2018 Guidelines

GUIDELINE  HEALTH SERVICES 

Recommendations on screening for breast cancer in women aged 40–74 years who are not at increased risk for breast cancer

Scott Klarenbach MD MSc, Nicki Sims-Jones RN MScN, Gabriela Lewin MD, Harminder Singh MD MPH, Gylène Thériault MD, Marcello Tonelli MD SM, Marion Doull PhD, Susan Courage RN BScN, Alejandra Jaramillo Garcia MSc, Brett D. Thombs PhD; for the Canadian Task Force on Preventive Health Care

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CMAJ Podcasts: interview in English at <https://soundcloud.com/cmajpodcasts/180463-guide-eng>; entrevue en français au <https://soundcloud.com/cmajpodcasts/180463-guide-fre>

See related article at www.cmaj.ca/lookup/doi/10.1503/cmaj.181538

Breast cancer mortality rates among Canadian women have declined from 41.7 per 100 000 in 1988 to an esti-

KEY POINTS



About Us

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About the CTFPHC

History

Members

Evidence Review and Synthesis Centres

Knowledge Translation Working Group

Meeting Minutes

The Canadian Task Force on Preventive Health Care was established by the Public Health Agency of Canada (PHAC) to develop clinical practice guidelines that support primary care providers in delivering preventive health care.

Guideline development is based on systematic analysis of scientific evidence.

The Task Force:

- Decides on the topics for which guidelines will be developed (or updated). Decisions are informed by consultation with PHAC and Health Canada, as well as professional health associations, health charities, academic institutions, guideline producers in other countries and other relevant parties.
- Directs the Evidence Synthesis Centres in the systematic review of scientific evidence according to key questions developed by the Task Force.
- Uses GRADE methodology for assessing strength of evidence based on best-practice scientific methods.
- Identifies when to involve experts in other disciplines to ensure the comprehensiveness of the analysis.
- Evaluates systematic review evidence to develop consensus recommendations.

Breast cancer screening: Part A. An evidence report to inform an update of the Canadian Task Force on Preventive Health Care 2011 Guideline

ABSTRACT

Background and Purpose:

The objectives of this evidence report were to synthesize up-to-date evidence on the benefits and harms of breast cancer screening for women who are ≥ 40 years old and not at high risk by conducting a modified overview of selected systematic reviews and an updated search for more recent primary studies. The findings will be used by the CTFPHC, along with additional considerations of feasibility, acceptability, affordability, and equity, to change or reaffirm previous recommendations.

Data Sources:

Eighteen pre-identified systematic reviews were considered for further assessment for inclusion for the overview of reviews. The search for primary studies was conducted from October 2014 to January 2017 for all screening modalities, except breast-self exam, which was from October 2010. For primary studies, we searched MEDLINE and the Cochrane Library and also supplemented with various grey literature sources. For false-positives, we relied on the Canadian Partnership against Cancer (CPAC) (cycle 2011-2012) report to calculate false-positive mammograms and biopsies on false positive data.

Study Selection:

The population of interest were women aged 40 or older who were not at high risk for breast cancer. The screening modalities of interest were the following compared to usual care/no screening: (i) mammography +/- clinical breast exam/breast self-exam; (ii) MRI +/- clinical breast exam/breast self-exam; (iii) ultrasound +/- clinical breast exam/breast self-exam; (iv): clinical breast exam alone; (v) breast self-exam alone. The outcomes of interest were breast cancer and all-cause mortality, overdiagnosis, and false positive mammograms and biopsies on false positives. Only randomized controlled trials (RCTs) were considered for mortality outcomes (breast cancer and all-cause). RCTs, controlled clinical trials and cohort studies were considered for the outcome of overdiagnosis.

Breast Cancer Screening: Part B. Systematic Review on Women's Values and Preferences to Inform an Update of the Canadian Task Force on Preventive Health Care 2011 Guideline

SUMMARY

Background and Purpose: CTFPHC recommendations are based on a systematic, structured, and transparent assessment of the balance of an intervention's potential benefits and harms, with explicit consideration of other relevant factors and integration of multidisciplinary input including that of stakeholders and patients/public. Our purpose was to systematically review studies providing information on women's values and preferences towards breast cancer screening, in terms of how they weigh the benefits and harms from screening that are considered by the CTFPHC to be most critical for their decision making (Key Question A). We also explored how, and to what extent, women use these outcome valuations when making decisions to undergo screening (Key Question B).

Data Sources and Selection: We searched four databases (MEDLINE, Cochrane Library, CINAHL, PsycINFO; to December 5, 2017), reference lists of systematic reviews and included studies, and several websites for studies, published in English or French and after 2000 beginnings of increased scrutiny about benefit-to-harm ratio from screening), where women were asked directly or indirectly (via screening intentions) about the relative importance placed on expected benefits and harms of breast-cancer screening using any modality for women at least 40 years of age and not at high-risk for breast cancer. We included studies of any design where authors had women consider at least one benefit (breast-cancer, all-cause mortality) and one harm (false positive recall [FPs], FPs leading to biopsy, overdiagnosis) rated as critically important by the CTFPHC for making decisions. Studies either needed to provide to participants some form of effect estimate for the outcomes, or have the objective of eliciting preference weights or trade-offs between frequencies of benefits and harms. Two reviewers independently screened titles and abstracts, and all citations considered relevant were retrieved in full text for further independent selection with a standard form with consensus or third reviewer input for disagreements. Reasons for exclusion at full text review were documented.

Source: <https://canadiantaskforce.ca/wp-content/uploads/2018/11/>

Womens-Values-and-Preferences-on-Breast-Cancer-Screening_FINAL.pdf

Beyond RCT evidence

Pan-Canadian study of mammography screening and mortality from breast cancer.

[Coldman A¹](#), [Phillips N¹](#), [Wilson C¹](#), [Decker K¹](#), [Chiarelli AM¹](#), [Brisson J¹](#), [Zhang B¹](#), [Payne J¹](#), [Doyle G¹](#), [Ahmad R¹](#).

+ Author information

Erratum in

J Natl Cancer Inst. 2015 Jan;107(1):dju404 doi:10.1093/jnci/dju404.

Abstract

BACKGROUND: Screening with mammography has been shown by randomized controlled trials to reduce breast cancer mortality in women aged 40 to 74 years. Estimates from observational studies following screening implementation in different countries have produced varied findings. We report findings for seven Canadian breast screening programs.

METHODS: Canadian breast screening programs were invited to participate in a study aimed at comparing breast cancer mortality in participants and nonparticipants. Seven of 12 programs, representing 85% of the Canadian population, participated in the study. Data were obtained from the screening programs and corresponding cancer registries on screening mammograms and breast cancer diagnoses and deaths for the period between 1990 and 2009. Standardized mortality ratios were calculated comparing observed mortality in participants to that expected based upon nonparticipant rates. A substudy using data from British Columbia women aged 35 to 44 years was conducted to assess the potential effect of self-selection participation bias. All statistical tests were two-sided.

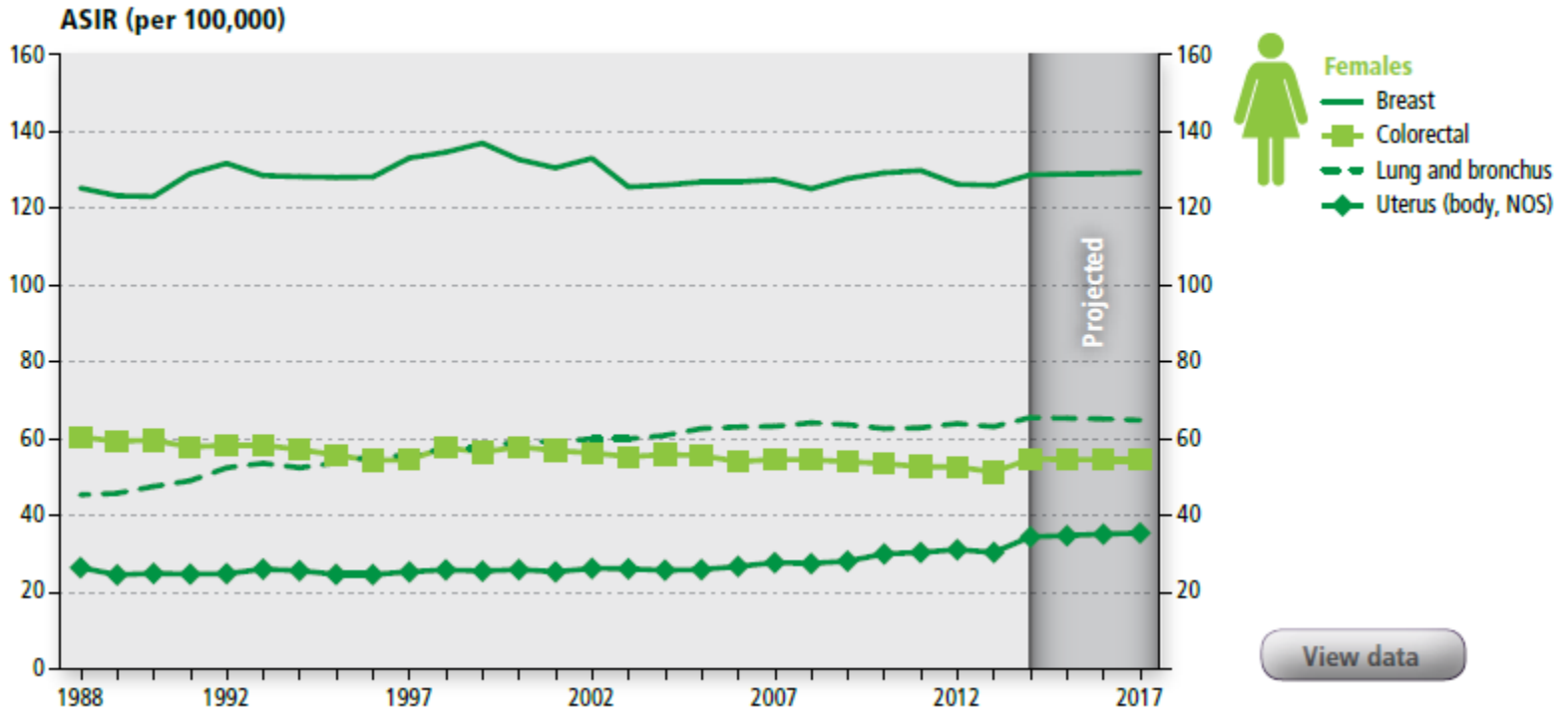
RESULTS: Data were obtained on 2796472 screening participants. The average breast cancer mortality among participants was 40% (95% confidence interval [CI] = 33% to 48%) lower than expected, with a range across provinces of 27% to 59%. Age at entry into screening did not greatly affect the magnitude of the average reduction in mortality, which varied between 35% and 44% overall. The substudy found no evidence that self-selection biased the reported mortality results, although the confidence intervals of this assessment were wide.

CONCLUSION: Participation in mammography screening programs in Canada was associated with substantially reduced breast cancer mortality.

Outcome

Incidence of Breast Cancer

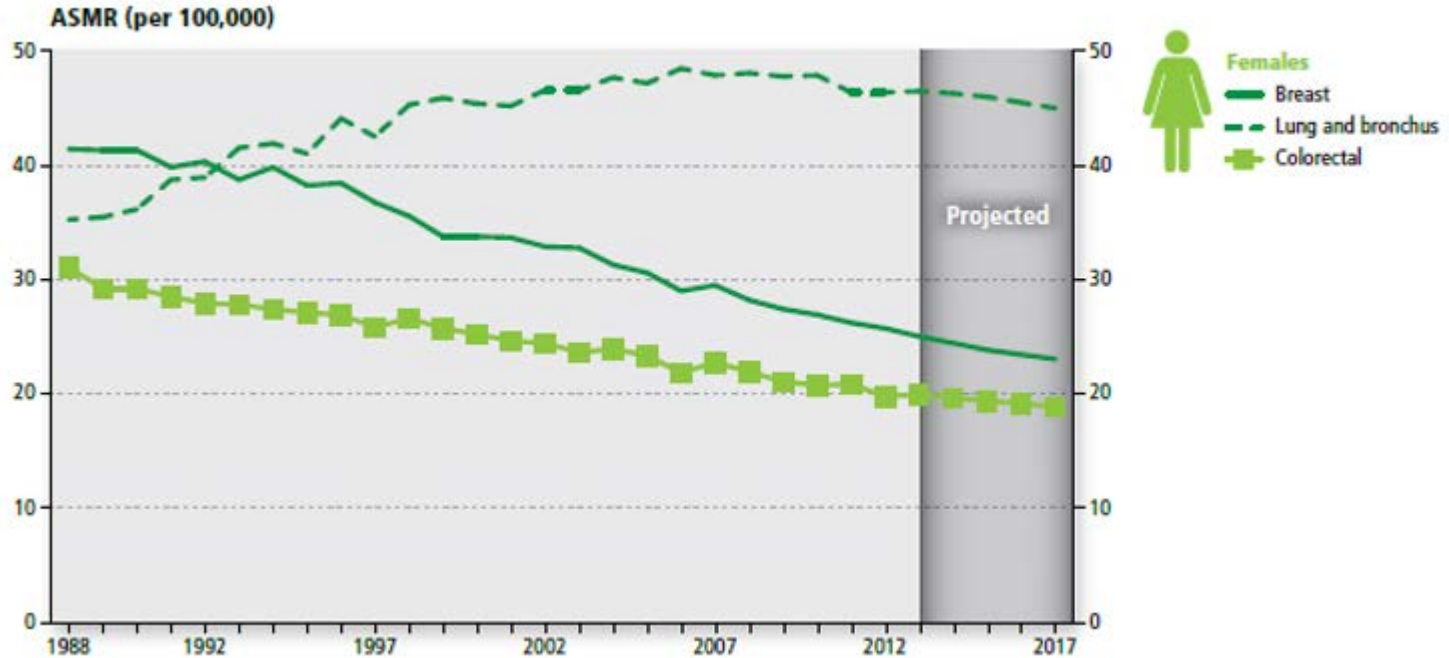
FIGURE 1.5 Age-standardized incidence rates (ASIR) for selected* cancers, females, Canada, 1988–2017



Source: Canadian Cancer Statistics 2017

'Benefits' of Screening

FIGURE 2.5 Age-standardized mortality rates (ASMR) for selected* cancers, females, Canada, 1988–2017



Source: Canadian Cancer Statistics 2017

Outcome




Mortality \approx Diagnosis (screening) + Treatment

* cumulative endpoint

* assumes standard for clinical pathway

Risk

Guidelines over the years - I

GUIDELINE  HEALTH SERVICES 

Recommendations on screening for breast cancer in women aged 40–74 years who are not at increased risk for breast cancer

Scott Klarenbach MD MSc, Nicki Sims-Jones RN MScN, Gabriela Lewin MD, Harminder Singh MD MPH, Guylène Thériault MD, Marcello Tonelli MD SM, Marion Doull PhD, Susan Courage RN BScN, Alejandra Jaramillo Garcia MSc, Brett D. Thombs PhD; for the Canadian Task Force on Preventive Health Care

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See related article at www.cmaj.ca/lookup/doi/10.1503/cmaj.181538

Breast cancer mortality rates among Canadian women have declined from 41.7 per 100 000 in 1988 to an esti-

KEY POINTS

Guidelines over the years - II

CMAJ

GUIDELINES

Recommendations on screening for breast cancer in average-risk women aged 40–74 years

The Canadian Task Force on Preventive Health Care

See related commentary by Gøtzsche on page 1957 and at www.cmaj.ca/lookup/doi/10.1503/cmaj.111721

Of the newly diagnosed cases of breast cancer in Canada, 80% were in women over the age of 50 years, and about 28% were in women aged 70 years or older (Figure 1),¹ with little variation by province. Regular screening for breast cancer with mammography, breast self-examinations and clinical breast examinations are widely recommended to reduce mortality due to breast cancer. Although controversy remains over precisely which screening services should be provided and to whom, these methods are frequently used in contemporary practice.²⁻⁴

Outcomes of screening for breast cancer such as tumour detection and mortality must be put into context of the harms and costs of false-

disease (defined as those with no previous breast cancer, no history of breast cancer in a first-degree relative, no known mutations in the *BRCA1/BRCA2* genes or no previous exposure of the chest wall to radiation). Recommendations are provided separately for women aged 40–49, 50–69 and 70–74 years and are aimed at clinicians and policy-makers. The recommendations are intended to inform both organized and opportunistic screening.

Methods

The Canadian Task Force on Preventive Health Care is an independent panel of clinicians and methodologists with expertise in prevention, pri-

Competing interests: Marcello Tonelli, Michel Joffres, James Dickinson, Harminder Singh, Gabriela Lewin and Richard Birtwhistle have received support for travel to meetings from the Public Health Agency of Canada. Gabriela Lewin is an employee of Kemptville District Hospital. No other competing interests were declared.

This article has been peer reviewed.

Correspondence to: The Canadian Task Force on Preventive Health Care,



Guidelines over the years - III



Cancer Care Ontario

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GUIDELINES & ADVICE

Breast Cancer Screening for Women at High Risk

Healthcare Provider FAQs

Genetics Clinic FAQs

The Ontario Breast Screening Program (OBSP) screens women ages 30 to 69 who are confirmed to be at high risk of developing breast cancer, once a year with a mammogram and breast magnetic resonance imaging (MRI) (or screening breast ultrasound if MRI is not medically appropriate). This kind of testing is based on scientific evidence and ensures that high risk women receive the benefits of organized screening.

Risk Factors for Breast Cancer

- Sex (female)
- Age
- Genetic predisposition (e.g., BRCA)
- Personal history of Breast Cancer
- Cancer treatment (chest wall irradiation)
- Family History
- Clinical risk factors:
 - ▶ Age at menarche, parity, age at first live birth, number of children, breastfeeding, breast density, oral contraceptives, hormone replacement therapy

Personalized Medicine

- Risk of Breast Cancer
- Screening Interval (yrs)
- Screening Modality (X-ray, MRI)



PERSONALIZED RISK ASSESSMENT FOR
PREVENTION & EARLY DETECTION OF BREAST CANCER:
INTEGRATION & IMPLEMENTATION

Jacques Simard

Project Leader
Canada Research Chair in Oncogenetics
Université Laval

Anna Maria Chiarelli

Co-Project Leader
Provincial Lead Scientist
Ontario Breast Screening Program
Cancer Care Ontario



The University of Manchester



RESEARCH STRATEGY – PERSPECTIVE I&I

OUR OVERARCHING GOALS ARE:

- To improve personalized risk assessment to offer **cost-effective risk-based screening and prevention** of breast cancer to women most likely to benefit.
- To determine the **optimal implementation approaches** within the Canadian healthcare system.

OUR PROJECT WILL PROVIDE:

Patient-oriented: A more accurate risk prediction improving genetic counselling of high risk women about screening and risk reduction strategies.

Population-oriented: Real-life evidence on how to shift from primarily age-based “*one-size fits all*” screening to risk-based approaches to improve the balance of benefits to harms.

RISK PROFILING

GENETIC RISK PROFILE

FAMILY HISTORY OF CANCER

DEMOGRAPHIC DATA

MAMMOGRAPHIC DENSITY

LIFESTYLE AND HORMONAL FACTORS

- Reproductive history
- BMI
- Height
- Alcohol
- Oral contraceptives



HIGH RISK



MODERATE RISK



GENERAL POPULATION RISK

PERSPECTIVE I&I



DALHOUSIE
UNIVERSITY

Inspiring Minds



**TAILORED BREAST SCREENING TO INDIVIDUAL RISK
(START/STOP AGE, FREQUENCY, MODALITIES) WILL LEAD TO:**



- Identifiable high risk women
- Early detection
- Survival
- Quality of life
- Prevention



- False positive screens
- Overdiagnosis/Overtreatment
- Invasive treatments
- Psychosocial impacts
- Clinical and economic burden

MAXIMIZE THE BENEFITS AND MINIMIZE THE HARMS

PERSPECTIVE I&I

Thank you!