**2022 MCGILL FAMILY MEDICINE REFRESHER COURSE**

# Approach to Breast Cancer Screening for Average and High Risk Patients

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Director, JGH Stroll Cancer Prevention Centre High Risk Breast Clinic

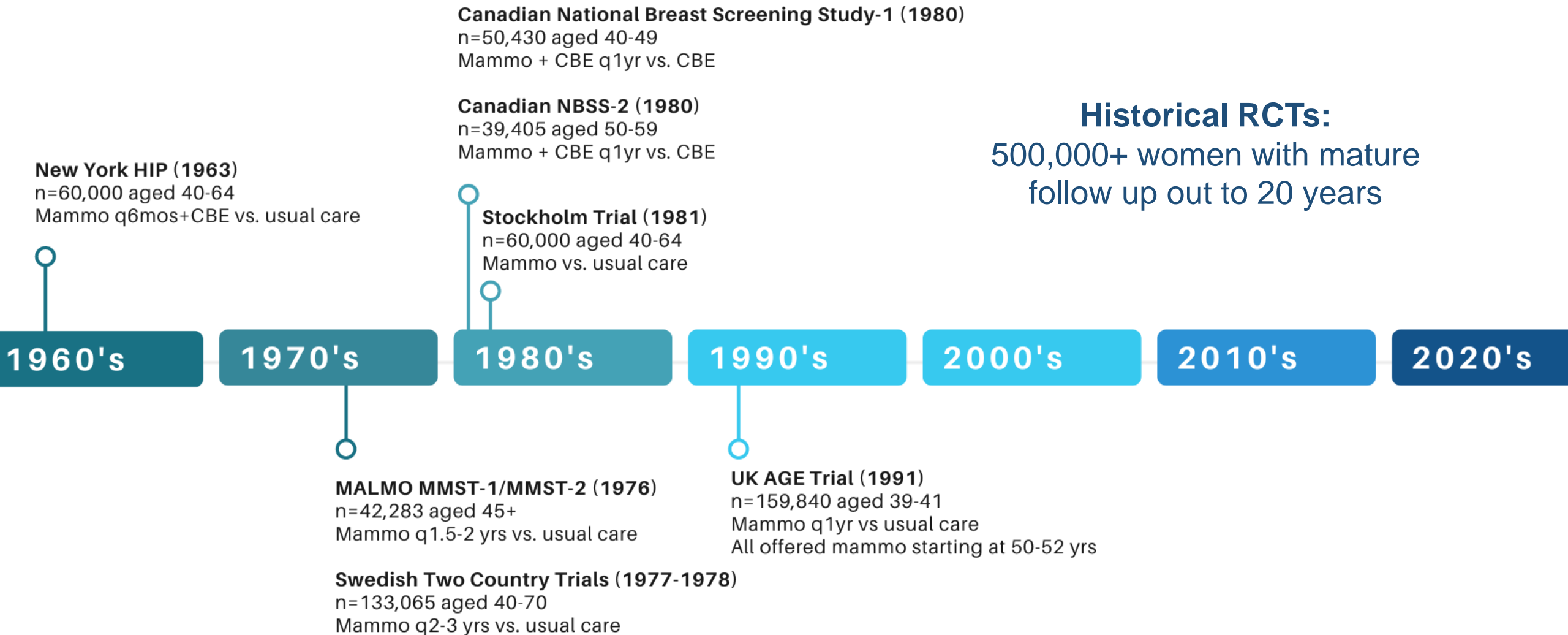Assistant Professor, McGill University Medical School

# No disclosures.

- The rationale behind breast cancer screening

- When should your patient start mammographic screening?

- Screening patients with dense breasts

- Screening patients with family history

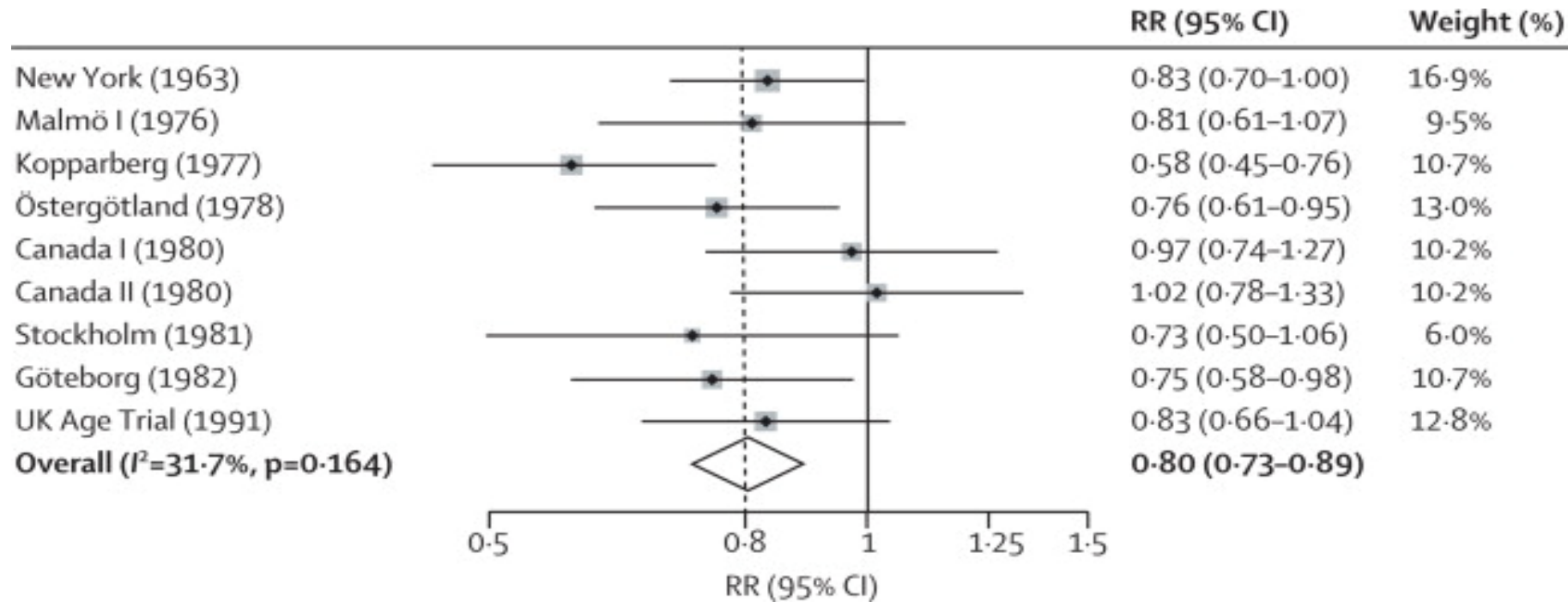- DBT: A new screening method you should know about

- **The rationale behind breast cancer screening**

- When should your patient start mammographic screening?

- Screening patients with dense breasts

- Screening patients with family history

- DBT: A new screening method you should know about

# One in eight Canadian women will develop breast cancer over the course of their lifetime

# Level I evidence that mammographic screening reduces breast cancer mortality by 20%

**Canadian National Breast Screening Study-1 (1980)**
n=50,430 aged 40-49
Mammo + CBE q1yr vs. CBE

**Canadian NBSS-2 (1980)**
n=39,405 aged 50-59
Mammo + CBE q1yr vs. CBE

**New York HIP (1963)**
n=60,000 aged 40-64
Mammo q6mos+CBE vs. usual care

**Stockholm Trial (1981)**
n=60,000 aged 40-64
Mammo vs. usual care

**Historical RCTs:**
500,000+ women with mature
follow up out to 20 years

1960's  1970's  1980's  1990's  2000's  2010's  2020's

**MALMO MMST-1/MMST-2 (1976)**
n=42,283 aged 45+
Mammo q1.5-2 yrs vs. usual care

**UK AGE Trial (1991)**
n=159,840 aged 39-41
Mammo q1yr vs usual care
All offered mammo starting at 50-52 yrs

**Swedish Two Country Trials (1977-1978)**
n=133,065 aged 40-70
Mammo q2-3 yrs vs. usual care

| | RR (95% CI) | Weight (%) |
|---|---|---|
| New York (1963) | 0·83 (0·70–1·00) | 16·9% |
| Malmö I (1976) | 0·81 (0·61–1·07) | 9·5% |
| Kopparberg (1977) | 0·58 (0·45–0·76) | 10·7% |
| Östergötland (1978) | 0·76 (0·61–0·95) | 13·0% |
| Canada I (1980) | 0·97 (0·74–1·27) | 10·2% |
| Canada II (1980) | 1·02 (0·78–1·33) | 10·2% |
| Stockholm (1981) | 0·73 (0·50–1·06) | 6·0% |
| Göteborg (1982) | 0·75 (0·58–0·98) | 10·7% |
| UK Age Trial (1991) | 0·83 (0·66–1·04) | 12·8% |
| Overall ($I^2$=31·7%, p=0·164) | 0·80 (0·73–0·89) | |

0·5    0·8    1    1·25    1·5

RR (95% CI)

**Pooled relative risk (RR) of 0.80 = 20% reduction in breast cancer mortality with mammographic screening**

Mammographic screening is the only imaging modality that has even been shown to reduce breast cancer related mortality

Mammographic screening is the foundation of breast screening on which all adjunct or supplemental imaging is added.
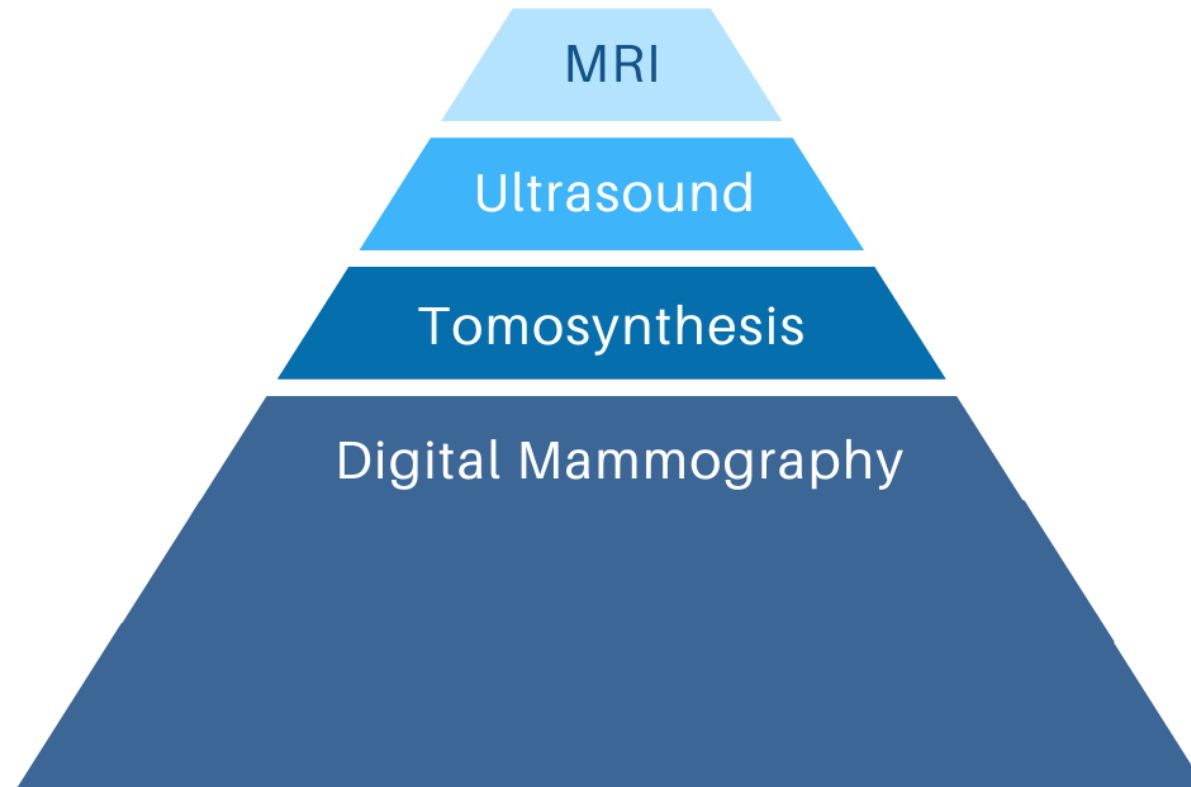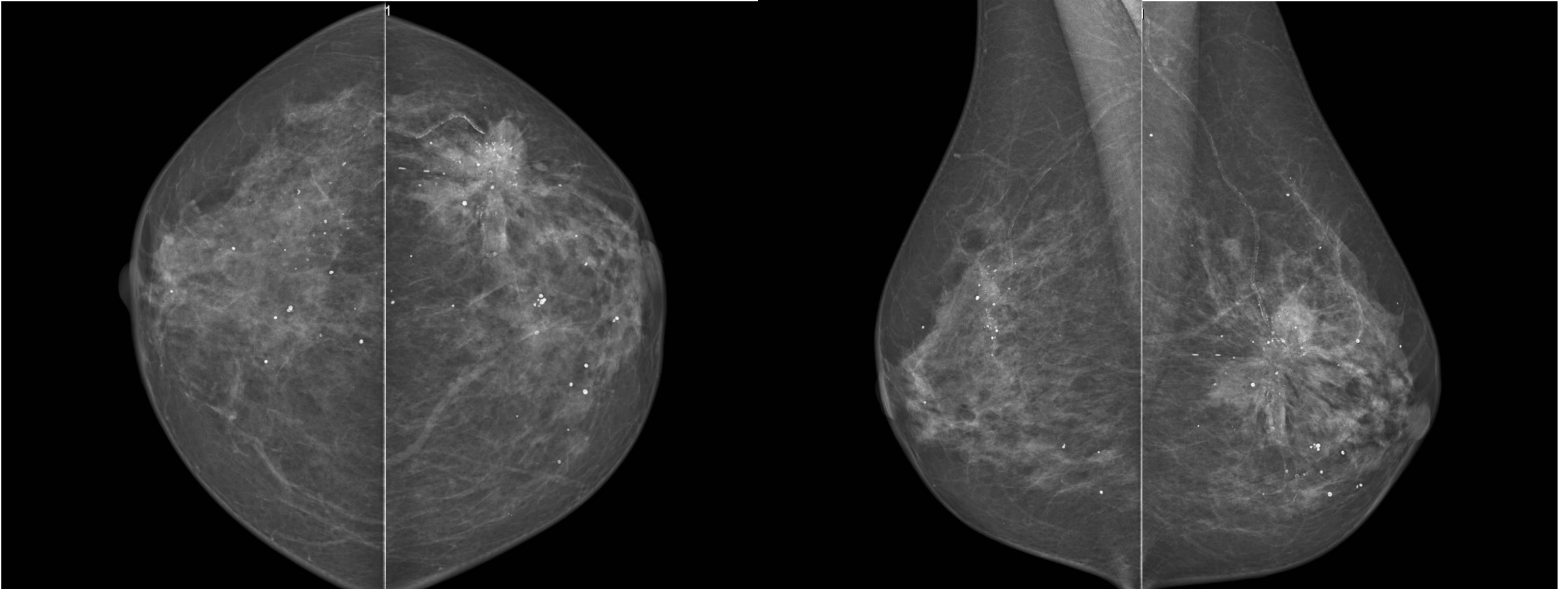
A mammogram is a 2D Xray taken of the breast using standard craniocaudal (CC) and mediolateral oblique (MLO) views

# A mammogram is a 2D Xray taken of the breast using standard craniocaudal (CC) and mediolateral oblique (MLO) views



Lateral / outer

*nipple

Medial / inner

L-MLO

Superior / upper

*nipple

Inferior / lower
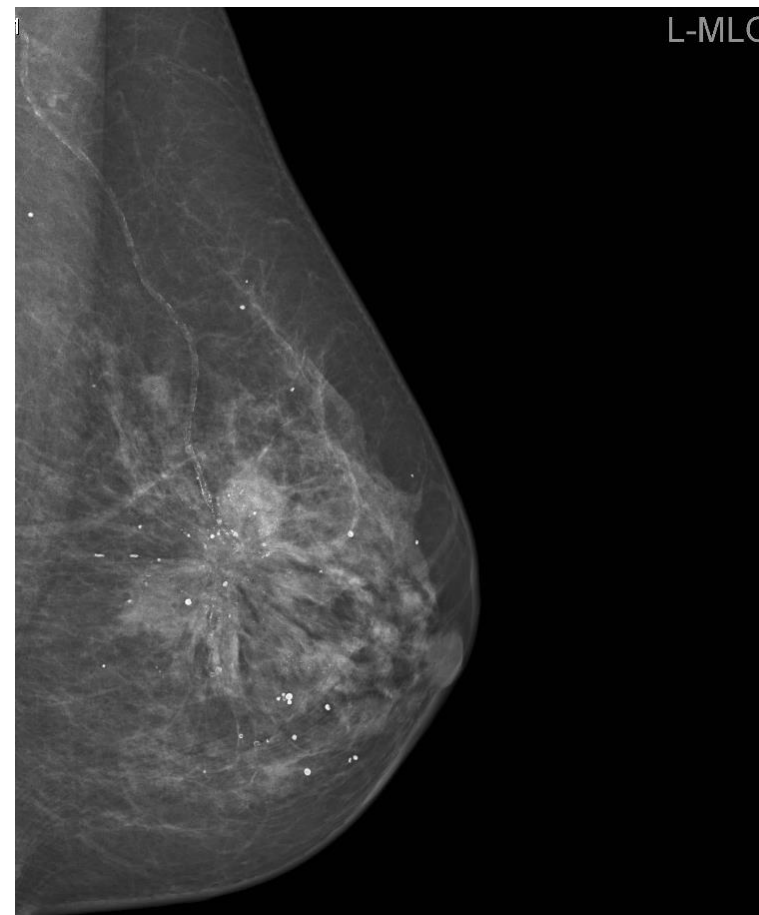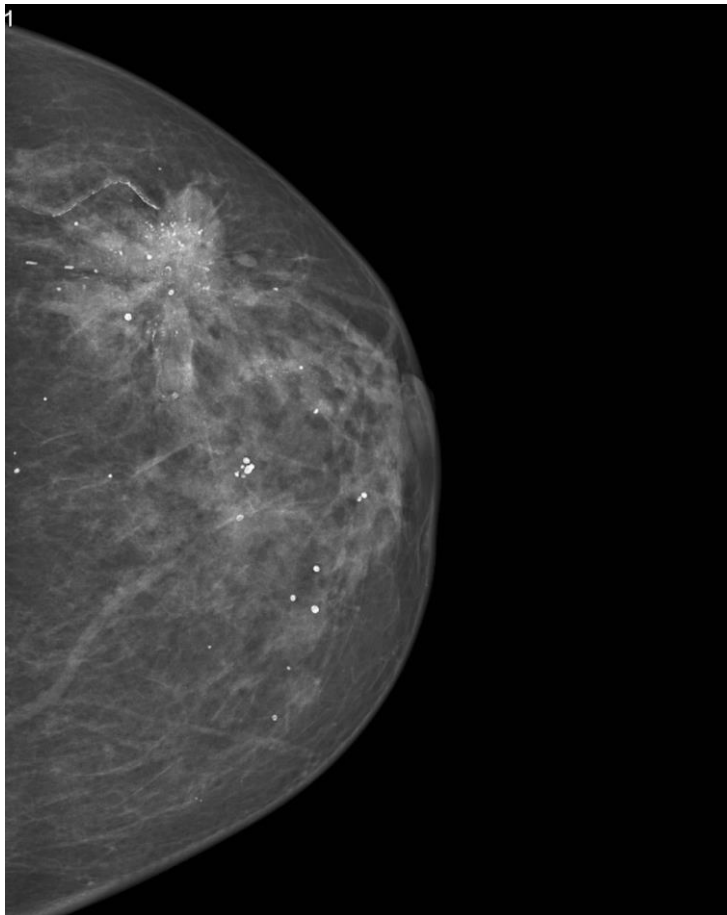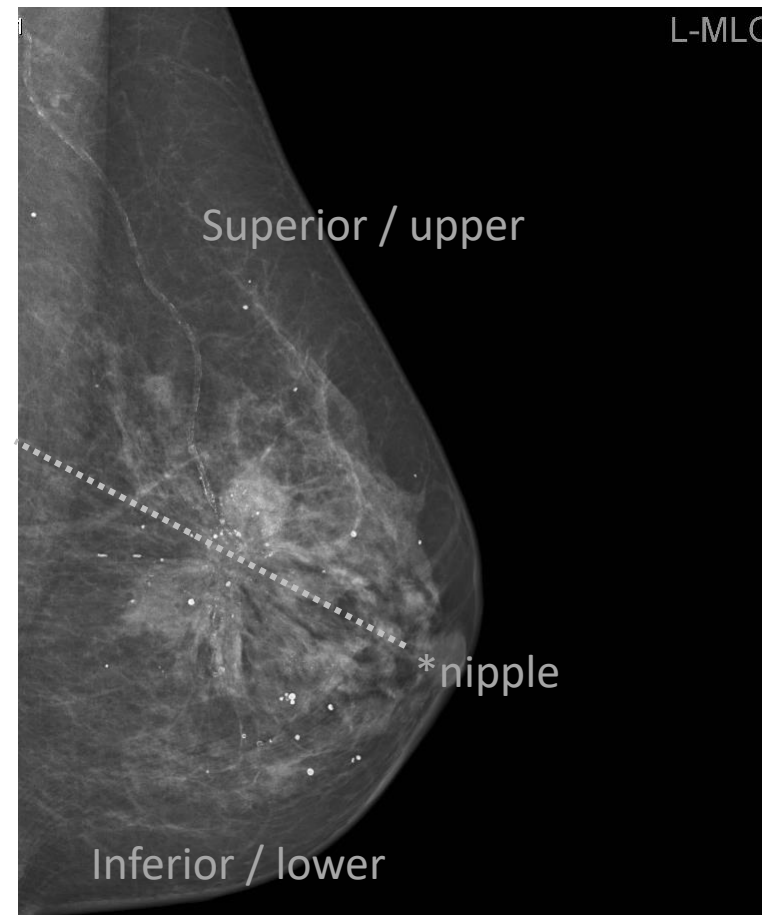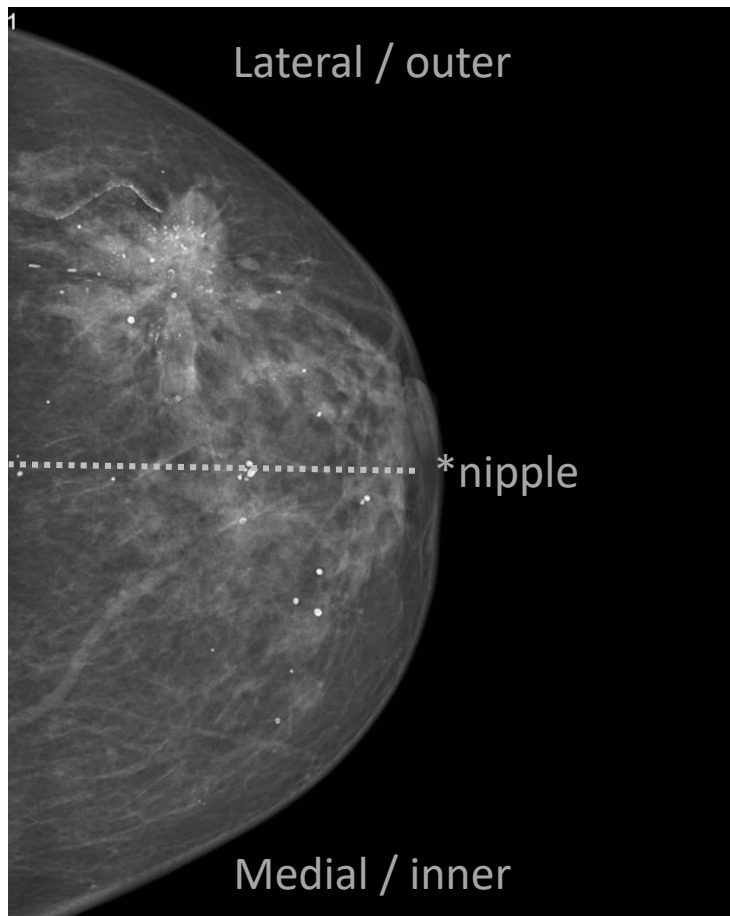
# Comparison to contralateral breast +/- prior imaging helpful

# When should your patient start screening?

# LEVEL OF RISK

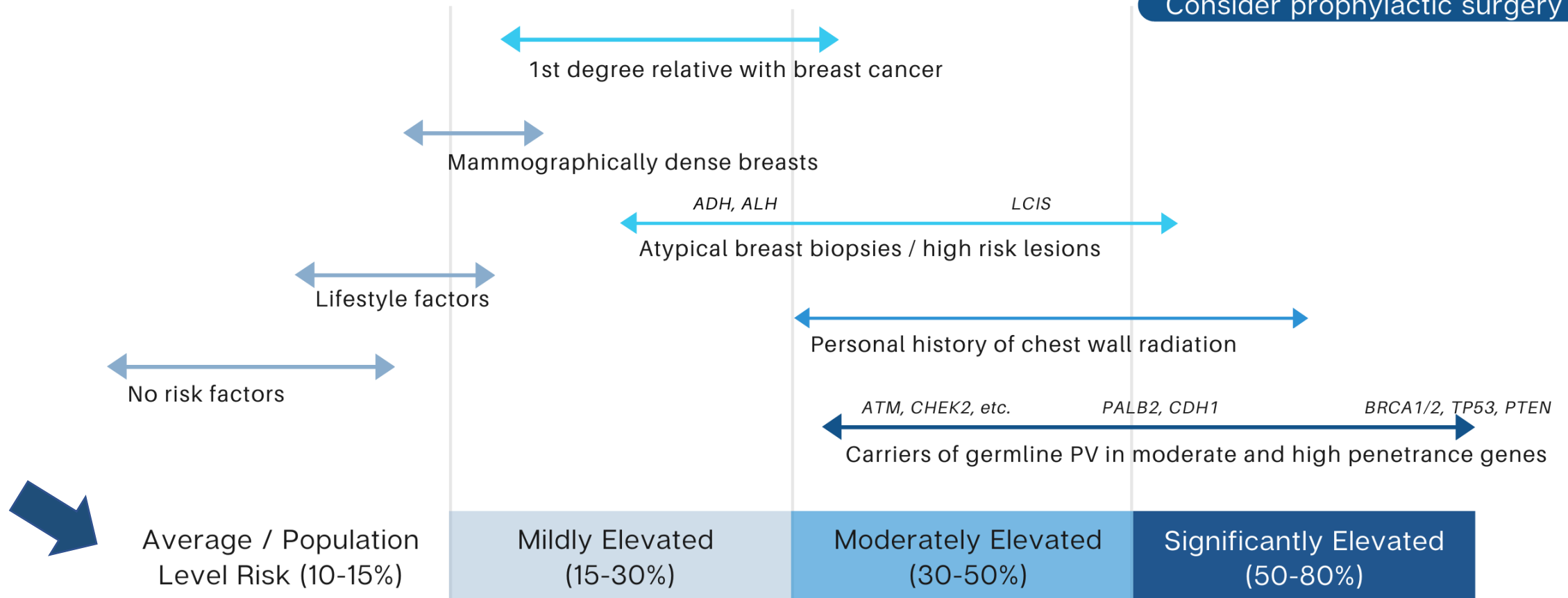## BREAST CANCER SCREENING

Clinical recommendations:

Increased surveillance

Consider endocrine prevention
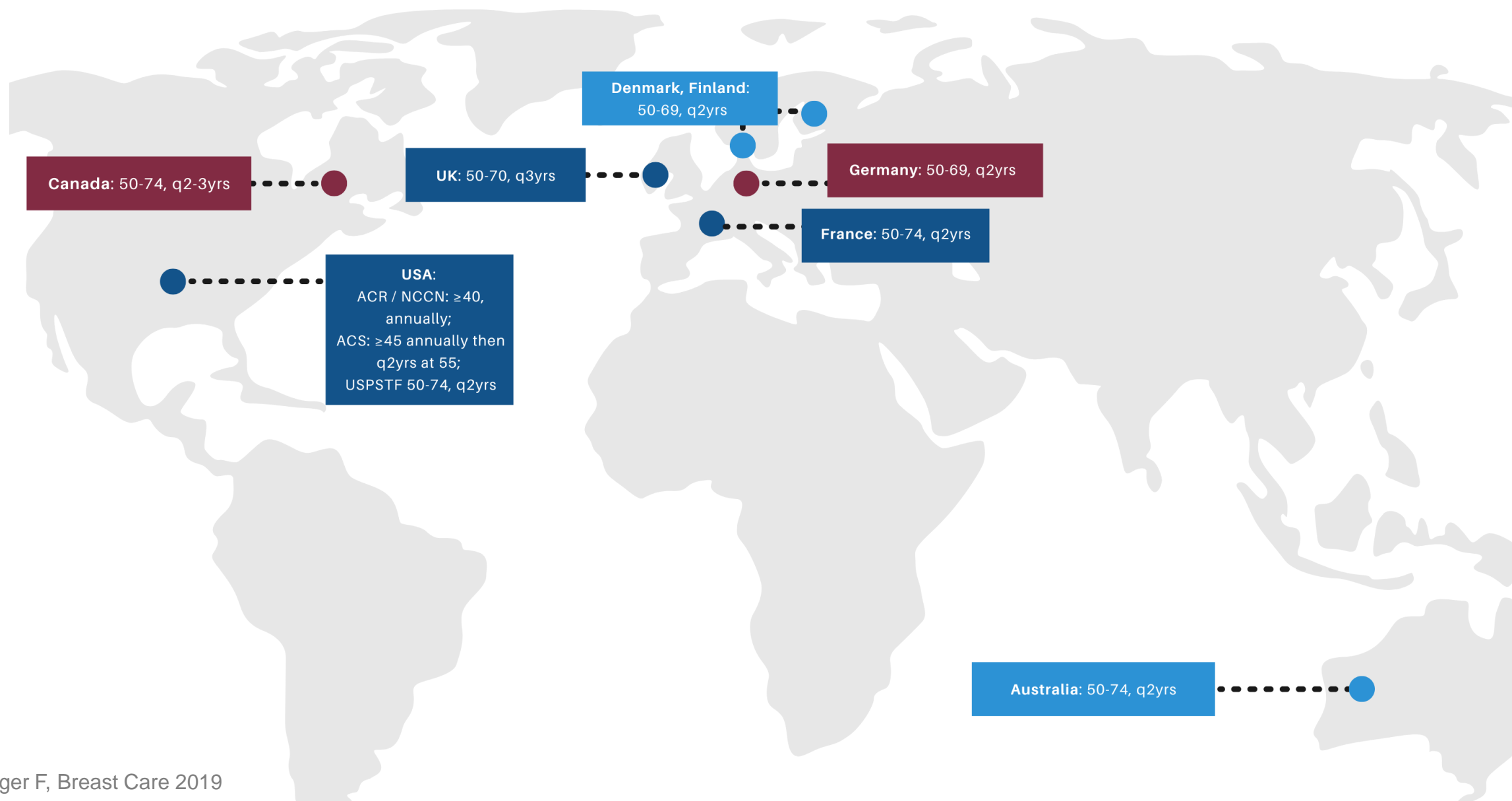
Consider prophylactic surgery

1st degree relative with breast cancer

Mammographically dense breasts

*ADH, ALH*                                    *LCIS*

Atypical breast biopsies / high risk lesions

Lifestyle factors

Personal history of chest wall radiation

No risk factors

*ATM, CHEK2, etc.*          *PALB2, CDH1*          *BRCA1/2, TP53, PTEN*

Carriers of germline PV in moderate and high penetrance genes

| Average / Population Level Risk (10-15%) | Mildly Elevated (15-30%) | Moderately Elevated (30-50%) | Significantly Elevated (50-80%) |
|---|---|---|---|

**Canadian Task Force
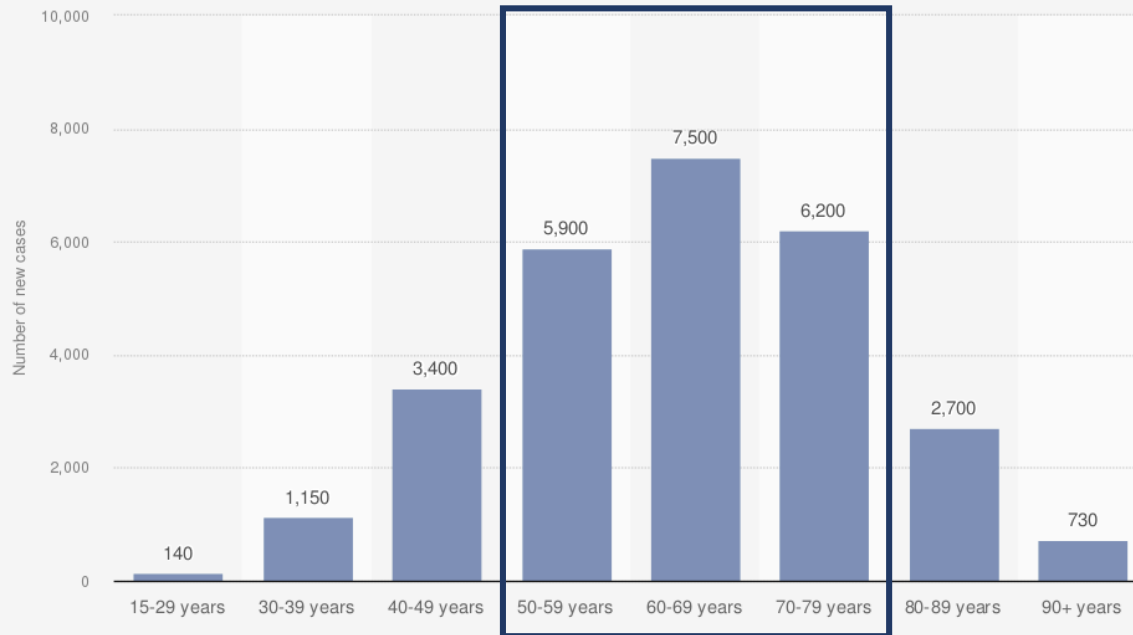on Preventive Health Care**

*"For women aged 50 to 74 years, we recommend screening with mammography every two to three years"*

GLOBAL SCREENING PROGRAMS          RECOMMENDATIONS FOR AGE & INTERVAL

Denmark, Finland: 50-69, q2yrs

Germany: 50-69, q2yrs

France: 50-74, q2yrs

Canada: 50-74, q2-3yrs

UK: 50-70, q3yrs

USA:
ACR / NCCN: ≥40, annually;
ACS: ≥45 annually then q2yrs at 55;
USPSTF 50-74, q2yrs

Australia: 50-74, q2yrs

Peintinger F, Breast Care 2019

Estimated number of new breast cancer cases among females in Canada by age group in 2021

- **Average age of Dx = 61 years**

- **83% BC diagnoses in Canada occur in women over 50 years**

- **Clinical and pathologic characteristics of BC differ in younger vs. older patients** (older patients = low grade, hormone-sensitive breast cancer; tend to be slow growing = more amenable to screen-detection)

Statistica 2022; StatCan (Canadian Cancer Registry)

| In 10,000 average risk women screened annually for 10 years… | From 40-49 years | From 50-59 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. over diagnosed | 28 | 44 | 66 |

Screening women between 50-70 is associated with the most benefit in terms of number of lives saved…

Keating NL et al. JAMA 2018

# …with tumors diagnosed at earlier stages



| 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) |

0.25   1.50   1.00   2.00

Favors Screening Group          Favors Control Group

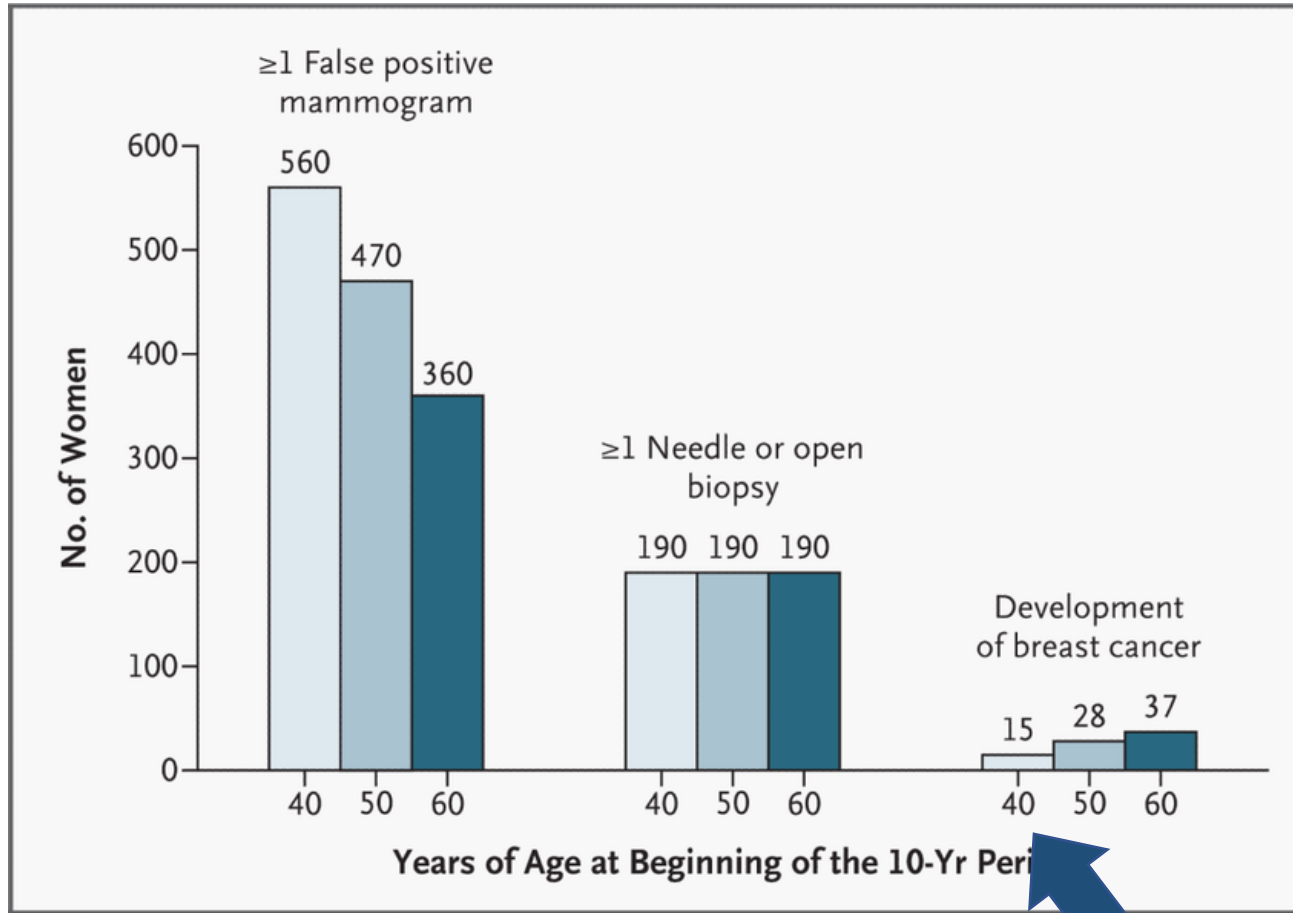What about average risk patients (no family history) who request screening at 40 years?

**Canadian Task Force on Preventive Health Care**

*"Some women aged 40 to 49 years may wish to be screened based on their values and preferences; in this circumstance, care providers should engage in shared decision-making with women who express an interest in being screened."*

Figure: Changes of FP, biopsies, and development of cancer among 1000 Women who undergo annual mammography for 10 years; Fletcher & Elmore, NEJM 2003

Sensitivity decreased due to dense breasts in 75% of women in this age group;
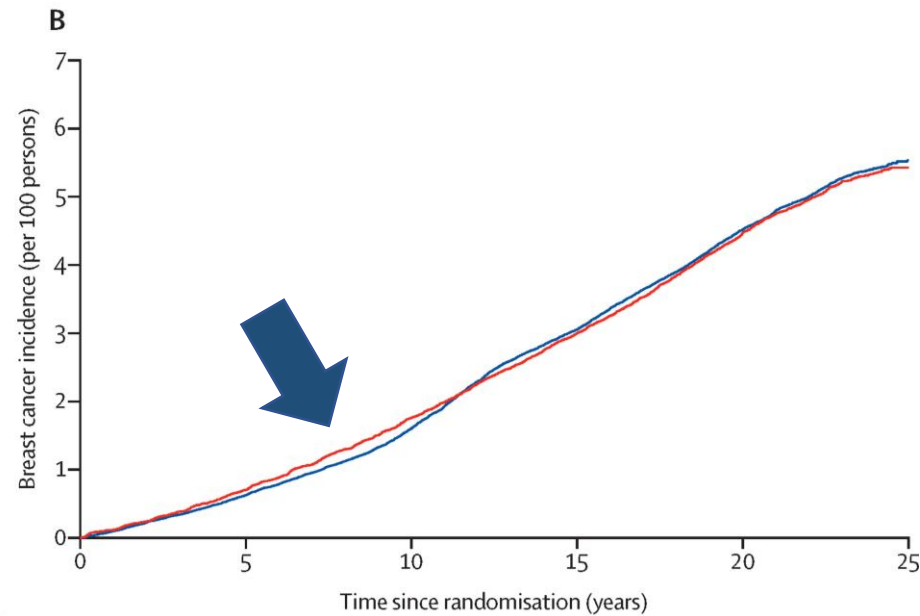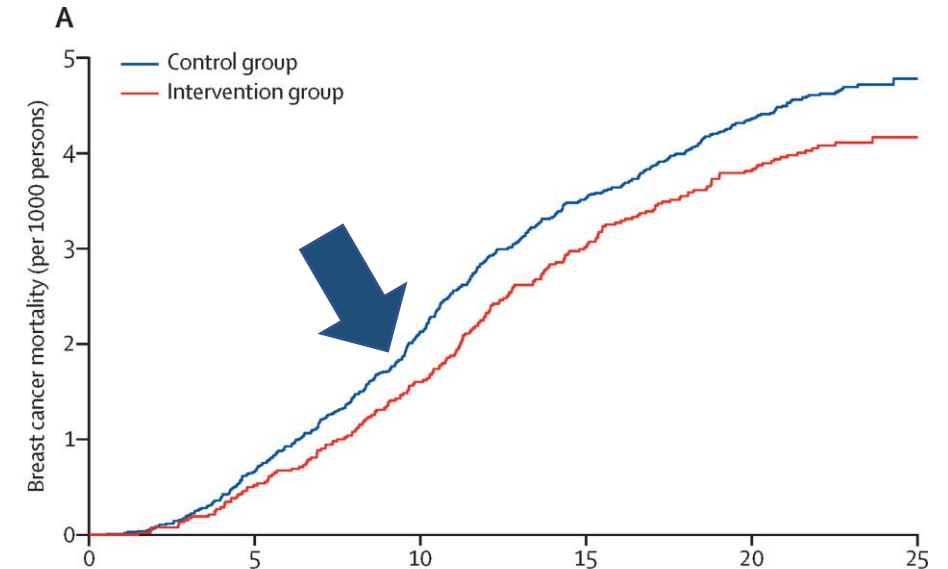
Increased call-backs and false positive biopsies;

10-year BC incidence lower in younger women = absolute benefit is lower overall;

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**Effect of mammographic screening from age 40 years on breast cancer mortality (UK Age trial): final results of a randomised, controlled trial**

Stephen W Duffy*, Daniel Vulkan*, Howard Cuckle, Dharmishta Parmar, Shama Sheikh, Robert A Smith, Andrew Evans, Oleg Blyuss, Louise Johns, Ian O Ellis, Jonathan Myles, Peter D Sasieni*, Sue M Moss*

**1960's**  **1970's**  **1980's**  **1990's**  **2000's**  **2010's**  **2020's**

**MALMO MMST-1/MMST-2 (1976)**
n=42,283 aged 45+
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Duffy et al., Lancet 2020

At 6-9 years post randomization, women in the screening group (red) were diagnosed with BC 8-12 months earlier than control group

There was a significant reduction in breast cancer mortality at 10 years follow up (RR 0.75, 95% CI 0.58-0.97) but this did not persist beyond 10 years; <1 death prevented/1000 women screened

Duffy et al., Lancet 2020

Mammographic screening reduces breast cancer mortality and leads to earlier detection in women over 50; the benefit of **annual mammography** for women aged 40-49 is less well established

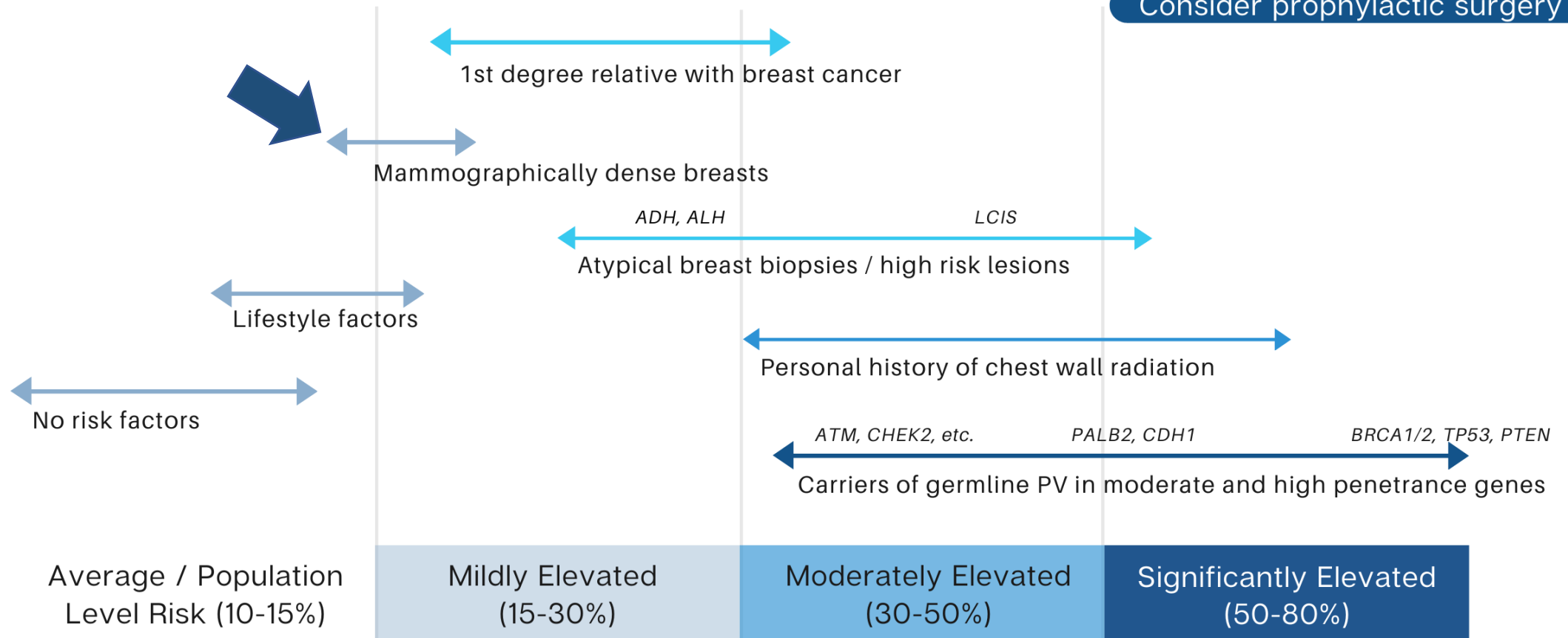What about patients with mammographically dense breasts?

**DENSE BREASTS** | **BREAST CANCER SCREENING**
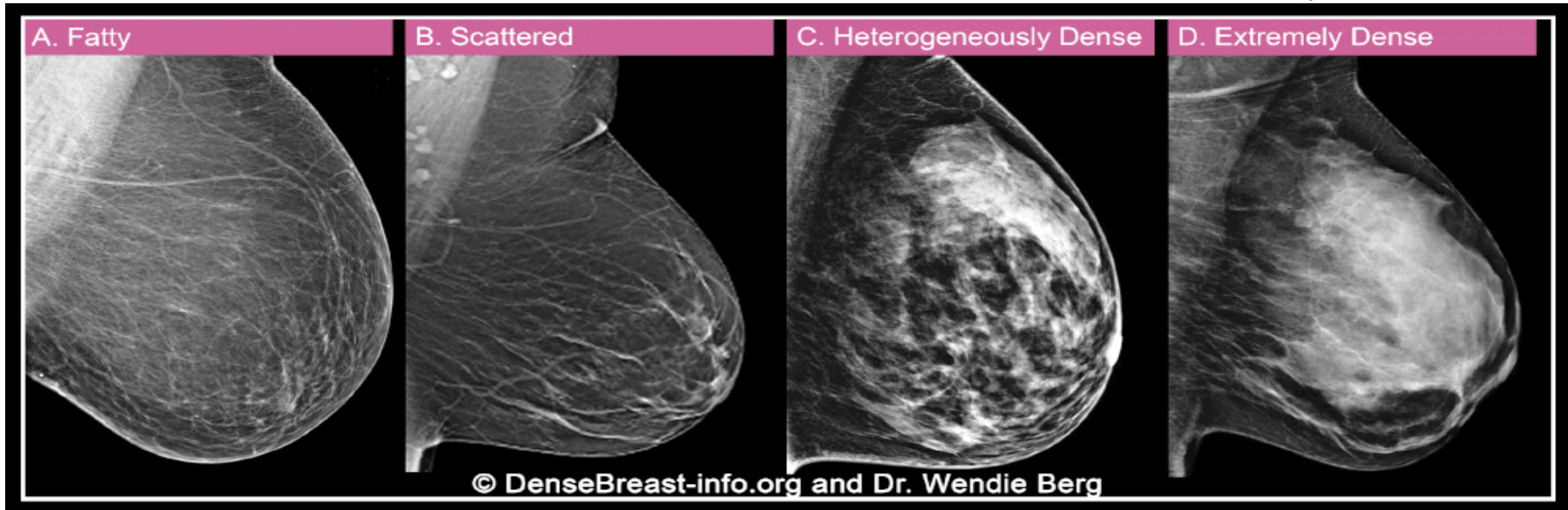
Clinical recommendations: Increased surveillance

Consider endocrine prevention

Consider prophylactic surgery

1st degree relative with breast cancer

Mammographically dense breasts

*ADH, ALH* — *LCIS*
Atypical breast biopsies / high risk lesions

Lifestyle factors

Personal history of chest wall radiation

No risk factors

*ATM, CHEK2, etc.* — *PALB2, CDH1* — *BRCA1/2, TP53, PTEN*
Carriers of germline PV in moderate and high penetrance genes

| Average / Population Level Risk (10-15%) | Mildly Elevated (15-30%) | Moderately Elevated (30-50%) | Significantly Elevated (50-80%) |
|---|---|---|---|

Not Dense: MG Sensitivity 80-98%[1]   "Dense" Breasts: MG Sensitivity 30-48%[1]



A. Fatty   B. Scattered   C. Heterogeneously Dense   D. Extremely Dense

© DenseBreast-info.org and Dr. Wendie Berg

Almost Entirely Fatty
ACR Type A
(10%)

Scattered Fibroglandular
ACR Type B
(40%)

Heterogeneously Dense
ACR Type C
(40%)

Extremely Dense
ACR Type D
(10%)

[1]Hooley RJ et al, Radiology 2012

**Lower Mammographic Breast Density**

Older age

Post-menopausal status

Higher BMI/weight gain

Tamoxifen/Aromatase inhibitors

Increased Breast Cancer Risk

Increased Mammographic Sensitivity

**Mammographic Breast Density**

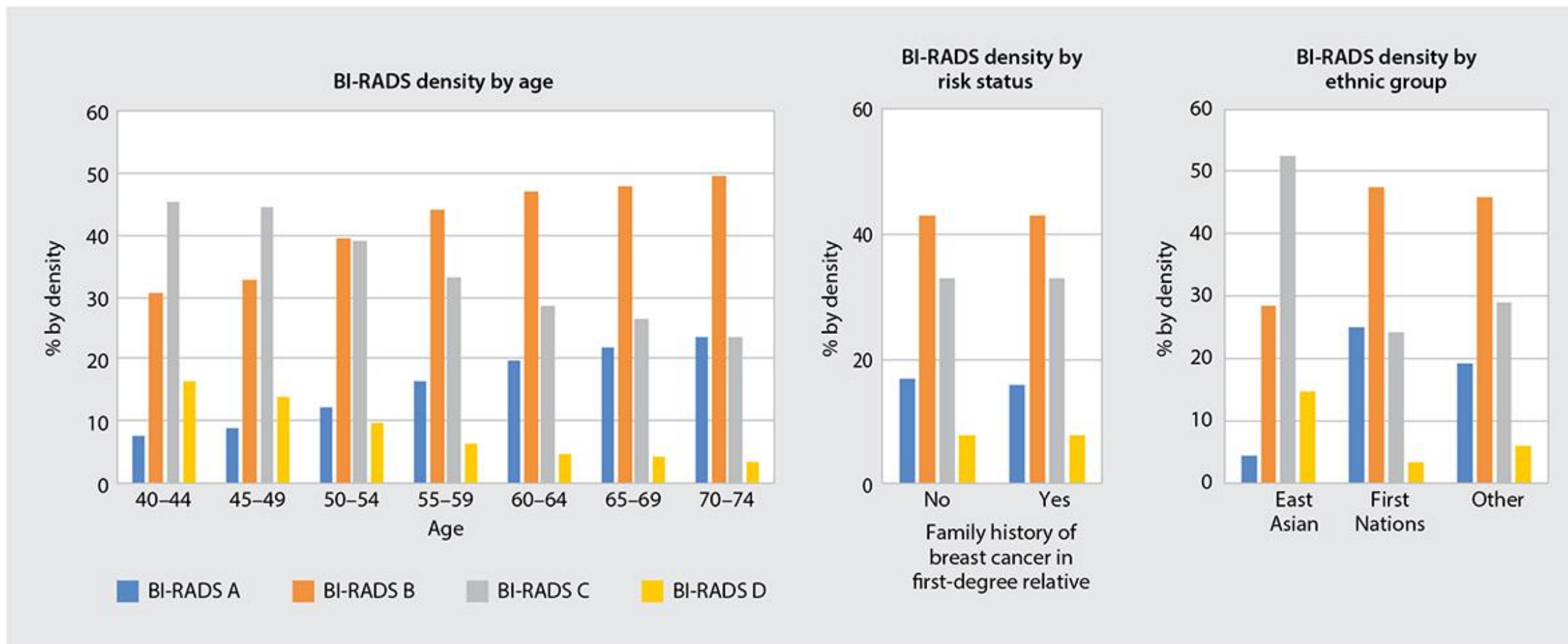Younger age

Pregnancy & lactation

HRT

Lower BMI/weight loss

Certain ethnicities

**FIGURE 3.** Breast density of participants screened in 2017 by age, risk status, and ethnic group.

Digital
Mammography

Digital
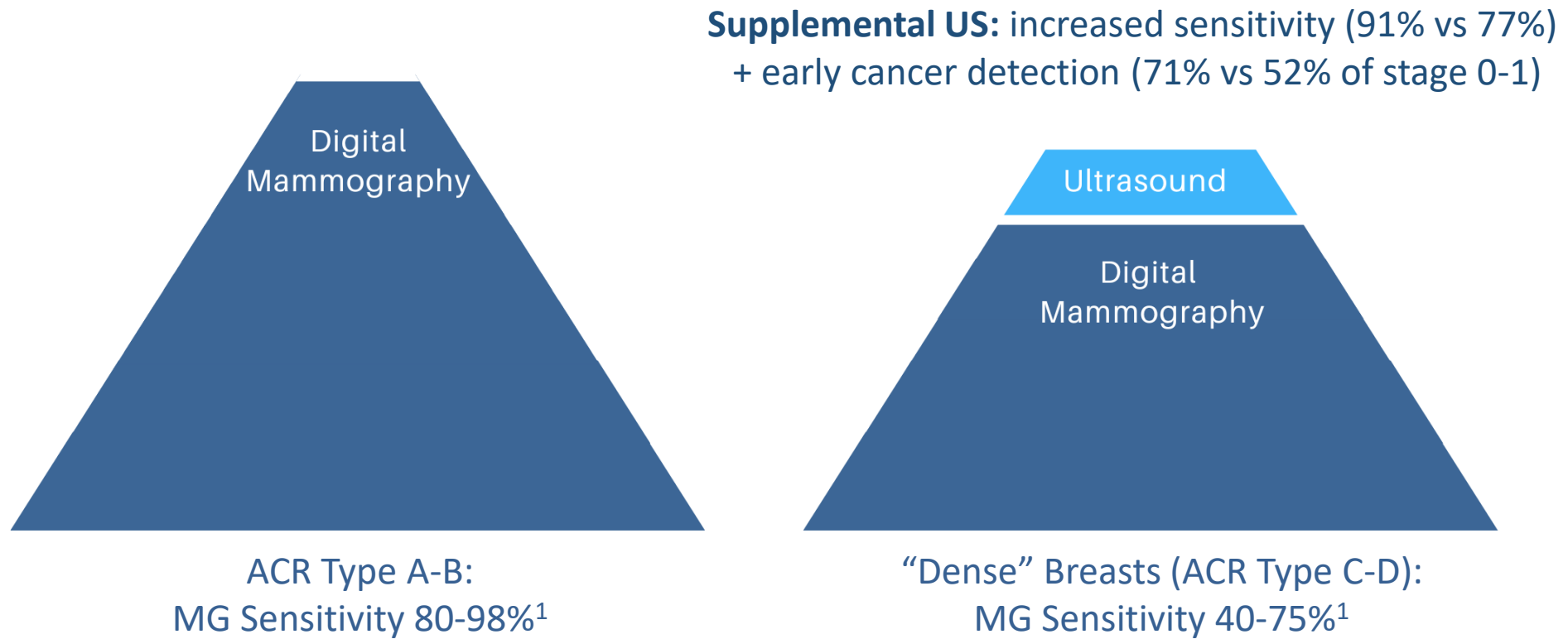Mammography

ACR Type A-B:
MG Sensitivity 80-98%[1]

"Dense" Breasts (ACR Type C-D):
MG Sensitivity 40-75%[1]

Hooley RJ et al, Radiology 2012; Ohuchi et al. Lancet 2016

**Supplemental US:** increased sensitivity (91% vs 77%)
+ early cancer detection (71% vs 52% of stage 0-1)

Digital Mammography

Ultrasound

Digital Mammography

ACR Type A-B:
MG Sensitivity 80-98%[1]

"Dense" Breasts (ACR Type C-D):
MG Sensitivity 40-75%[1]

Tagliofico et al. EJC 2018; Berg et al. JAMA 2012; Ohuchi et al. Lancet 2016

| Risk Factor | Lifetime Risk | Age of onset | Screening modality | Frequency |
|---|---|---|---|---|
| No risk factors (Average risk) | 13% | 50 years | MG | Biennial |
| Dense breasts | 15-18% | 50 years | MG + US | Biennial |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

Women with dense breasts benefit from **MG + supplemental US** to increase the sensitivity of each screen. In the absence of other risk factors, they do not require more frequent screening. When or if breast density decreases (ie. over time), they can de-escalate to **MG alone.**
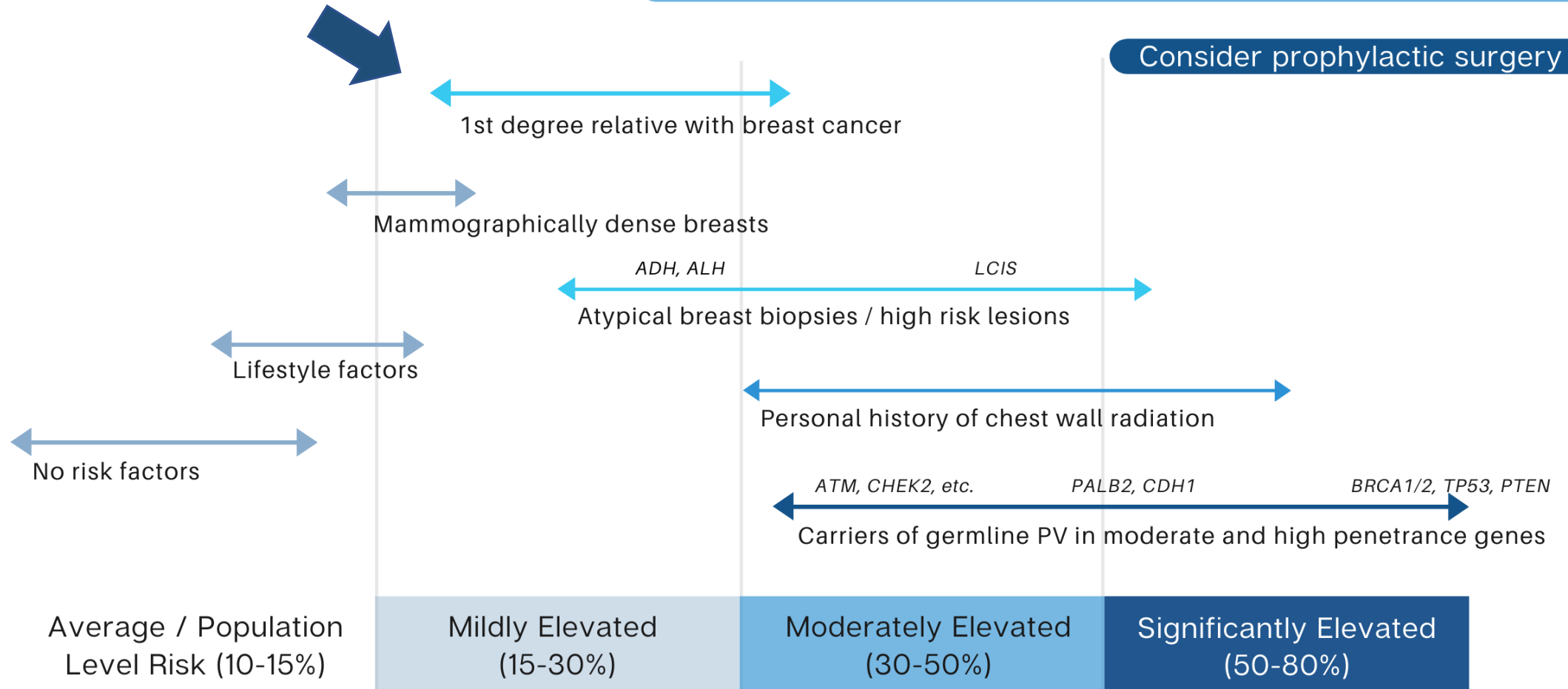
What about patients with a family history?

Clinical recommendations:

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Atypical breast biopsies / high risk lesions

Lifestyle factors

Personal history of chest wall radiation

No risk factors

*ATM, CHEK2, etc.*      *PALB2, CDH1*      *BRCA1/2, TP53, PTEN*

Carriers of germline PV in moderate and high penetrance genes

| Average / Population Level Risk (10-15%) | Mildly Elevated (15-30%) | Moderately Elevated (30-50%) | Significantly Elevated (50-80%) |
|---|---|---|---|

Patients with a **family history***, are recommended to initiate **annual mammography 10 years prior** to the earliest diagnosis of breast cancer in the family or at **age 40**, whichever comes first.

(*Strong FHx: mother or sister with breast cancer, or two or more 1st or 2nd degree relatives with breast cancer)

| Risk Factor | Lifetime Risk | Age of onset | Screening modality | Frequency |
|---|---|---|---|---|
| No risk factors (Average risk) | 13% | 50 years | MG | Biennial |
| Dense breasts | 15-18% | 50 years | MG + US | Biennial |
| Family history | 18-40% | 40 years / 10-years prior to first diagnosis in family[a] | MG +/- US if dense | Annual |
| | | | | |
| | | | | |
| | | | | |
| | | | | |

[a] Whichever occurs first (starting at 30 years at the earliest);

**"Any" family history ≠ strong family history**

Ie. In a larger family with 8 women, 1 affected woman with breast cancer represents population-level risk

Based on a family history of breast cancer:

**…in a mother dx at 45 and sister dx at 50 years: 39% (strong FHx)**

**…in a mother OR a sister dx at 50 years: 31% (strong FHx)**

…in 1 of 1 maternal aunts dx at 50 years: 22%

…in a paternal or maternal grandmother dx at 50 years: 21%

…in a maternal cousin (daughter of unaffected aunt) dx at 50 years: 16%

…in a maternal cousin (daughter of 1 of 4 healthy aunts) dx at 50 years: 14%

Clinical recommendations:

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Consider prophylactic surgery

1st degree relative with breast cancer

Mammographically dense breasts

*ADH, ALH*             *LCIS*

Atypical breast biopsies / high risk lesions

Lifestyle factors

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| Risk Factor | Lifetime Risk | Age of onset | Screening modality | Frequency |
|---|---|---|---|---|
| No risk factors (Average risk) | 13% | 50 years | MG | Biennial |
| Dense breasts | 15-18% | 50 years | MG + US | Biennial |
| Family history | 18-40% | 40 years / 10-years prior to first diagnosis in family[a] | MG +/- US if dense | Annual |
| Atypical breast biopsies (ADH, ALH, LCIS) | 20-40% | 50 years / following atypical breast biopsy | MG +/- US if dense | Annual |
| Moderate penetrance carriers (*CHEK2, ATM*) | 30-40% | 30-40 years | MG +/- US or MRI[c] | Annual / q6 months |
| Chest wall radiation under 30 years (Lymphoma) | 30-50% | 25 years / 8 years following exposure[b] | MG + MRI | Alternating q6 months |
| High penetrance carriers (*BRCA1/2, PALB2, TP53*) | 50-70% | 25 years (MRI only until 30) | MG + MRI | Alternating q6 months |

[a] Whichever occurs first (starting at 30 years at the earliest); [b] Whichever occurs later; [c] Insufficient evidence for or against MRI;
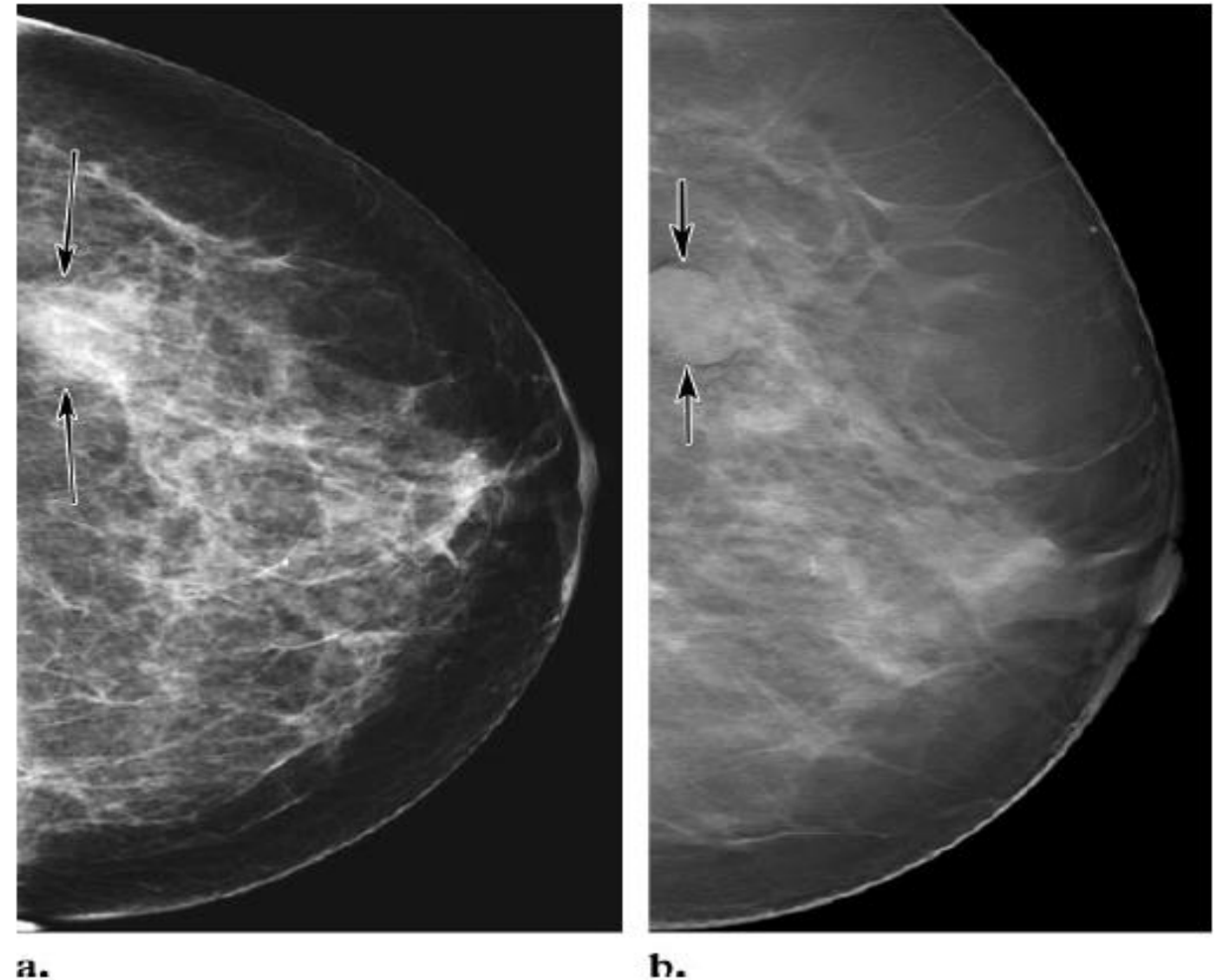
# Digital Breast Tomosynthesis

Position Statement on the Utilization of Digital Breast Tomosynthesis in Mammography Screening

*"Predicted to be the future for screening mammography and replace 2D digital mammography"* - CSBI

FDA approved in 2011. By 2020, 40% of accredited MG units & 72% of all certified breast imaging facilities in US

Recent European guidelines suggest women with dense breasts may benefit the most from DBT screening

In Canada, there has been a CSBI recommendation to switch/upgrade to DBT units when it is time to replace end of life mammography units



a.

b.

Ratanaprasatporn et al, Radiographics 2019; Canadian Society of Breast Imaging 2021
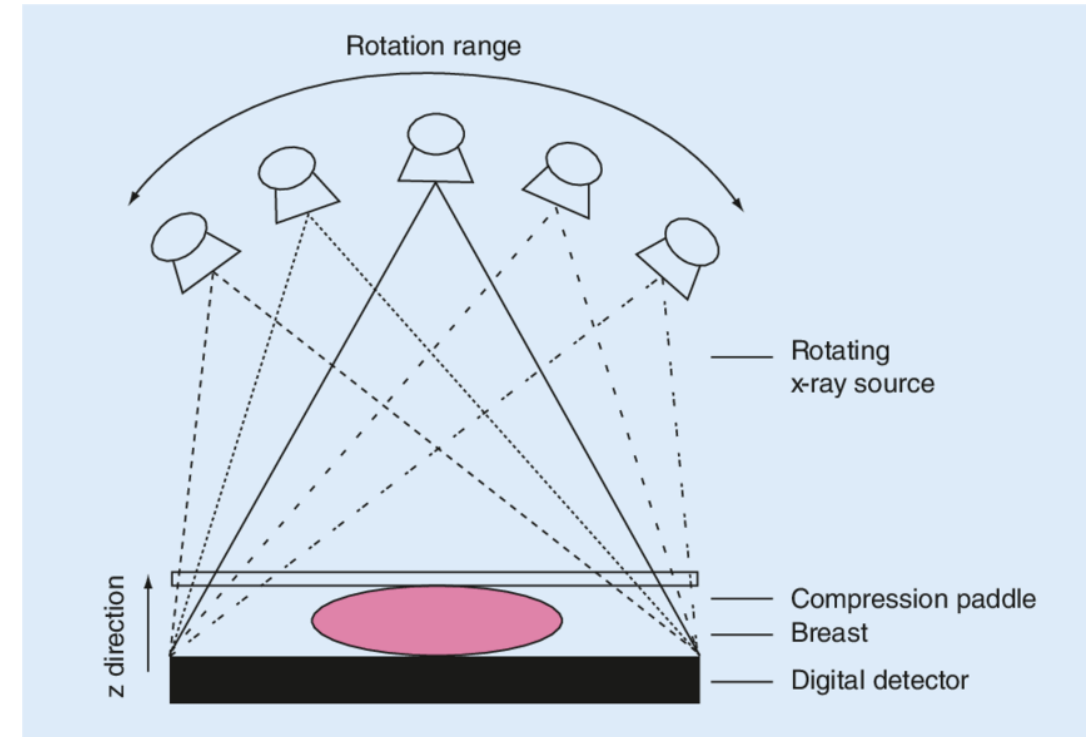
"Ability to diminish the effects of overlapping tissue by displaying one thin section of tissue at a time, resulting in improved detection and evaluation"

Mi Park et al, Radiographics 2007; Canadian Society of Breast Imaging 2021

**Table 1: Screening Outcomes with Combined DBT and DM Compared with DM Alone in Representative Retrospective Studies Published in 2013–2016**

| Study and Year | No. of Examinations | | Cancer Detection Rate | | | Recall Rate | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | DBT/DM | DM | DBT/DM* | DM* | P Value | DBT/DM[†] | DM[†] | P Value |
| Rose, 2013 (9) | 9499 | 13856 | 5.4 | 4.0 | .07 | 5.5 | 8.7 | <.001 |
| Haas, 2013 (10) | 6100 | 7058 | 5.7 | 5.2 | .7 | 8.4 | 12 | <.01 |
| Greenberg, 2014 (11) | 23149 | 54684 | 6.3 | 4.9 | .0056 | 13.6 | 16.2 | <.0001 |
| McCarthy, 2014 (12) | 15571 | 10728 | 5.5 | 4.6 | .02 | 8.8 | 10.4 | <.001 |
| Friedewald, 2014 (13) | 173663 | 281187 | 5.4 | 4.2 | <.001 | 9.1 | 10.7 | <.001 |
| Durand, 2015 (14) | 8591 | 9364 | 5.9 | 5.7 | .88 | 7.8 | 12.3 | <.0001 |
| Lourenco, 2015 (15) | 12921 | 12577 | 5.4 | 4.6 | .44 | 6.4 | 9.3 | <.0001 |
| McDonald, 2015 (16) | 15571 | 10728 | 5.4 | 4.6 | .41 | 8.8 | 10.4 | <.001 |
| Sharpe, 2016 (17) | 5703 | 80149 | 5.4 | 3.4 | .0001 | 6.1 | 7.5 | <.018 |
| Conant, 2016 (18) | 559998 | 142883 | 5.9 | 4.4 | .0026 | 8.7 | 10.4 | <.0001 |
| All | 830766 | 623214 | | . . . | . . . | | . . . | . . . |

Note.—Numbers in parentheses are reference number. Study populations may overlap in studies from the same institution.
*Number per 1000 examinations.
[†]Numbers are percentages.

Gao et al, Radiographics 2021
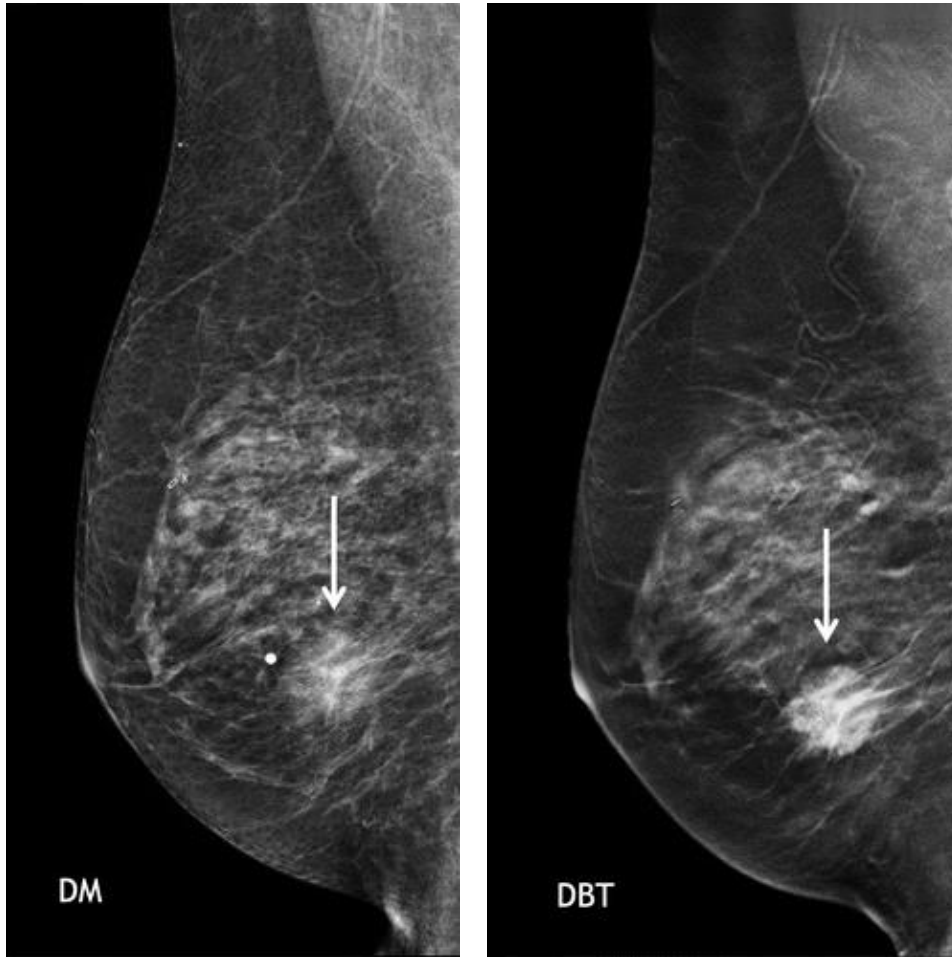
"DBT improves the cancer detection rate to a greater extent in Europe and Scandinavia (biennial screening) but reduces recall rates to a greater extent in the United States (higher baseline recall rate)"

Gao et al, Radiographics 2021; Marinovich JNCI 2021;
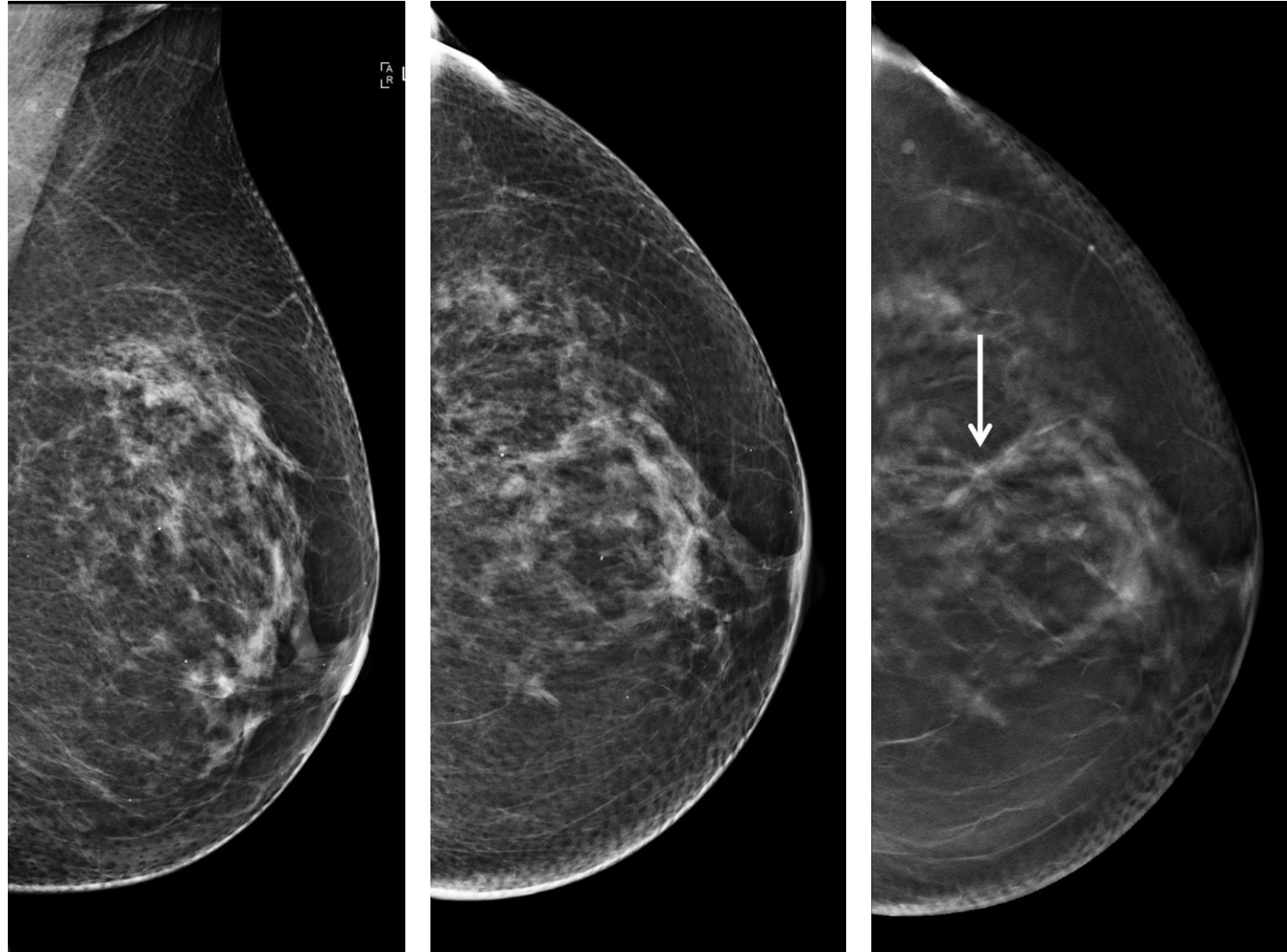
Small spiculated grade 1 node-negative ER+/PR+/HER2− invasive ductal carcinoma in a 62-year-old woman. **(a, b)** Mediolateral oblique **(a)** and craniocaudal **(b)** two-dimensional mammograms show that the tumor is occult. **(c)** In-plane craniocaudal DBT image shows that the tumor is visible (arrow)

## Advantages

Increased detection invasive cancers

Decreased recall rates / false positives

Decreased BIRADS 3 lesions requiring short interval follow up

Similar/lower detection of microcalcifications / DCIS (no overdiagnosis)

Cost-effective for medical system with lower out of pocket costs for patients
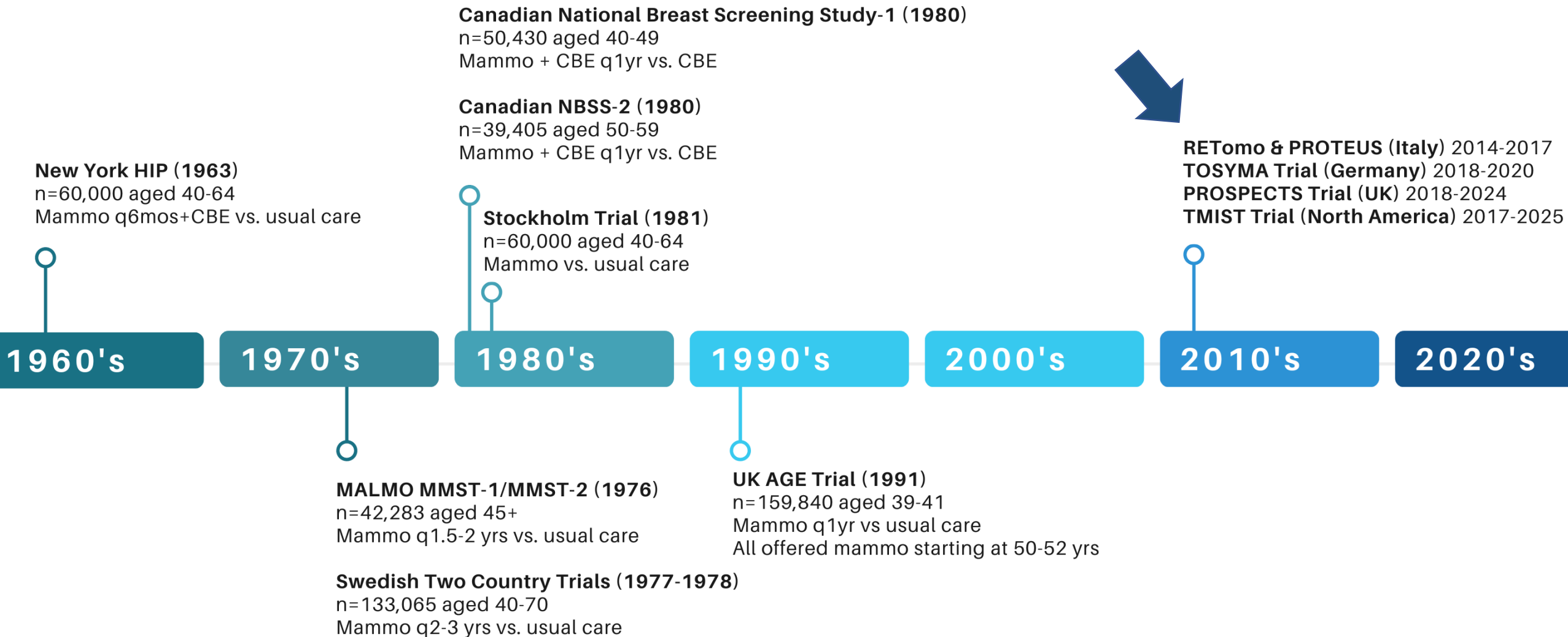
## Disadvantages

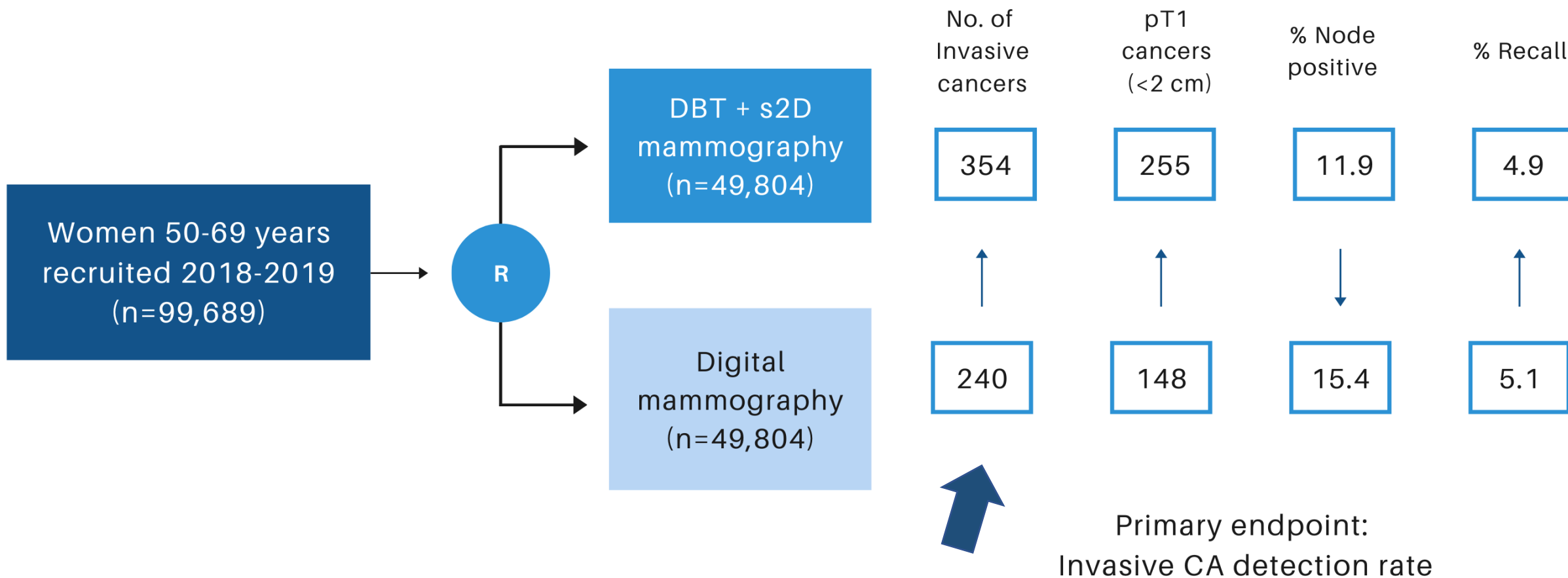Increased radiation if standard DM + DBT performed together

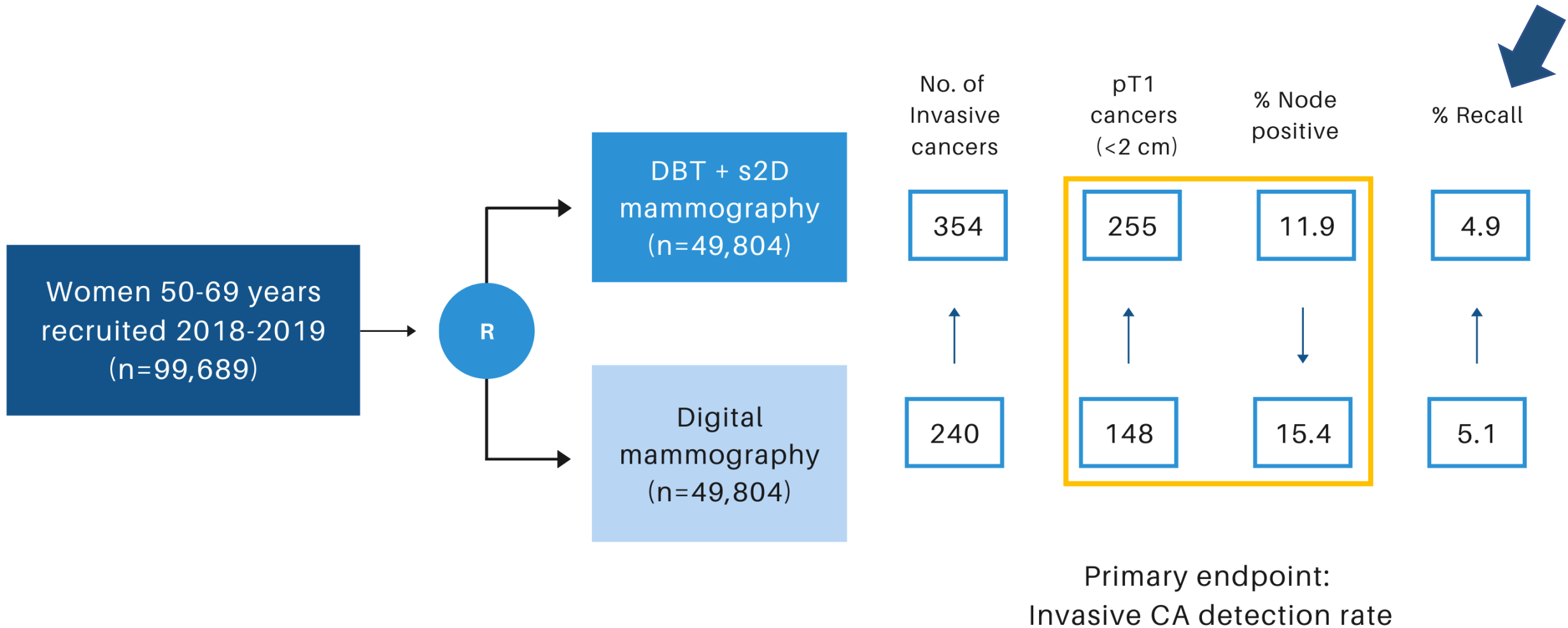Increased interpretation time (2.8 vs. 1.9 min)

No level 1 evidence from RCTs supporting mortality benefit

**Canadian National Breast Screening Study-1 (1980)**
n=50,430 aged 40-49
Mammo + CBE q1yr vs. CBE

**Canadian NBSS-2 (1980)**
n=39,405 aged 50-59
Mammo + CBE q1yr vs. CBE

**New York HIP (1963)**
n=60,000 aged 40-64
Mammo q6mos+CBE vs. usual care

**RETomo & PROTEUS (Italy)** 2014-2017
**TOSYMA Trial (Germany)** 2018-2020
**PROSPECTS Trial (UK)** 2018-2024
**TMIST Trial (North America)** 2017-2025

**Stockholm Trial (1981)**
n=60,000 aged 40-64
Mammo vs. usual care

| 1960's | 1970's | 1980's | 1990's | 2000's | 2010's | 2020's |
|---|---|---|---|---|---|---|

**MALMO MMST-1/MMST-2 (1976)**
n=42,283 aged 45+
Mammo q1.5-2 yrs vs. usual care

**UK AGE Trial (1991)**
n=159,840 aged 39-41
Mammo q1yr vs usual care
All offered mammo starting at 50-52 yrs

**Swedish Two Country Trials (1977-1978)**
n=133,065 aged 40-70
Mammo q2-3 yrs vs. usual care

Women 50-69 years recruited 2018-2019 (n=99,689)

**R**

DBT + s2D mammography (n=49,804)

Digital mammography (n=49,804)

| No. of Invasive cancers | pT1 cancers (<2 cm) | % Node positive | % Recall |
|---|---|---|---|
| 354 | 255 | 11.9 | 4.9 |
| 240 | 148 | 15.4 | 5.1 |

Primary endpoint:
Invasive CA detection rate

Heindl et al, Lancet Oncol 2022

GERMAN TOSYMA RCT — DIGITAL BREAST TOMOSYNTHESIS

Women 50-69 years recruited 2018-2019 (n=99,689)

R

DBT + s2D mammography (n=49,804)

Digital mammography (n=49,804)

| | No. of Invasive cancers | pT1 cancers (<2 cm) | % Node positive | % Recall |
|---|---|---|---|---|
| DBT + s2D | 354 | 255 | 11.9 | 4.9 |
| Digital | 240 | 148 | 15.4 | 5.1 |

Primary endpoint:
Invasive CA detection rate

Heindl et al, Lancet Oncol 2022

**TMIST »**

Women 45-74 presenting for screening 2017-2030 (n=128,905)

**R**
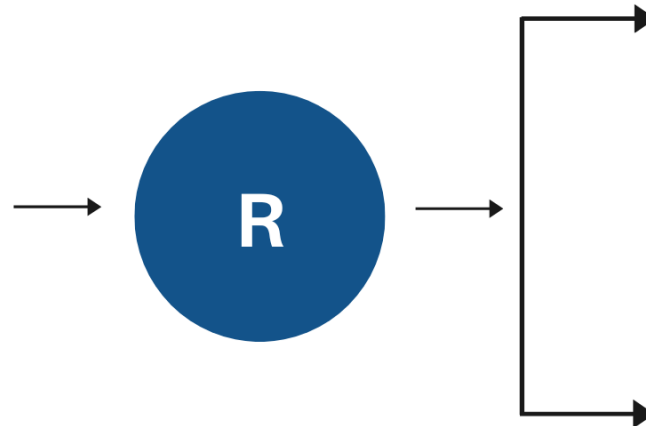
Tomosynthesis annually or biennially

Digital mammography annually or biennially

1° endpoint: Advanced cancers (node+ or >2cm) or small aggressive cancers (HER2+/TNBC) at 4.5 yrs FU

**If pre-menopausal = annual;**
**If post-menopausal with dense breasts or HRT or 1st degree FHx = annual;**
**All other patients or 74+ with FHx = biennial.**

**ECOG-ACRIN, NCI** and **CCTG** sponsored with 132 participating institutions;
**Canadian institutions:** BCCA-Vancouver Cancer Centre, Saint Joseph's Health Centre, Ottawa Hospital and Cancer Center, Odette Cancer Centre-Sunnybrook Health Sciences Centre, Mount Sinai Hospital, Hopital Du Sacre-Coeur de Montreal, CHU de Quebec-Hopital du Saint-Sacrement (HSS)
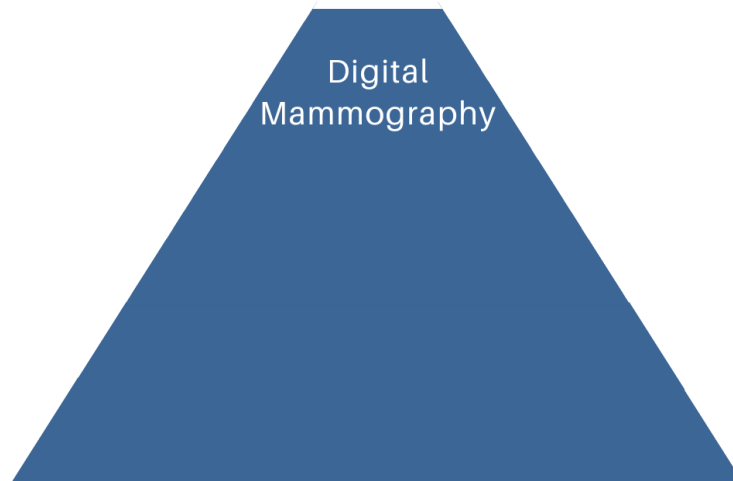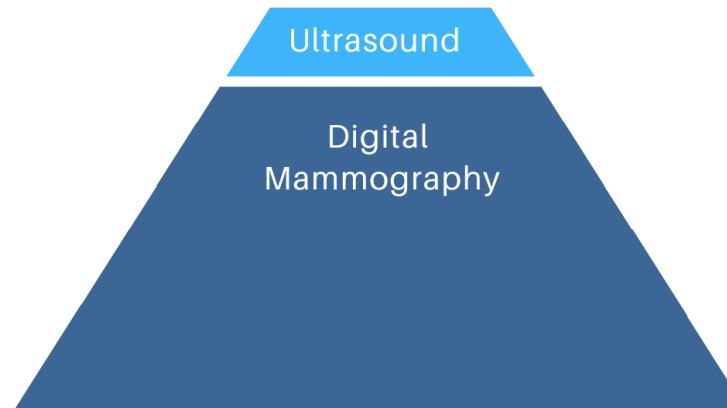
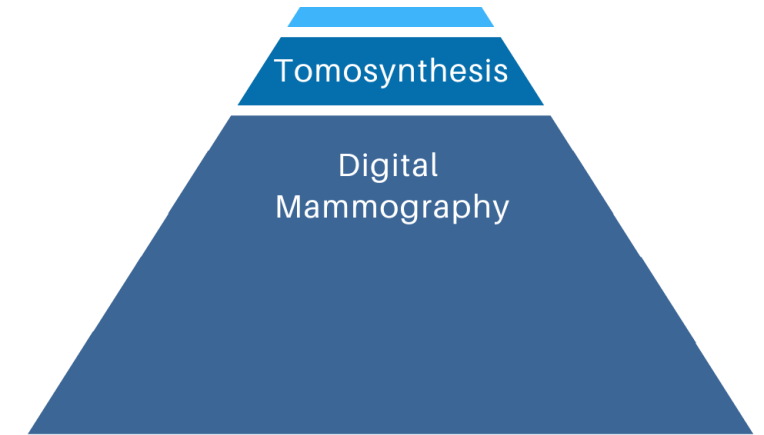**Digital breast tomosynthesis** is likely to become the new standard of care for breast cancer screening and will increase cancer detection while **decreasing recall rates,** which will be particularly beneficial in women with **dense breasts.**

McGILL FAMILY MEDICINE REFRESHER COURSE 2022

# Thank you!

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🐦 stephaniemwong