



Breast health

Dr Marième Sy, MD, ULB

H.U.B

HÔPITAL UNIVERSITAIRE
DE BRUXELLES
ACADEMISCH ZIEKENHUIS
BRUSSEL



17/01/2026

The causes of breast cancer are presumably **multifactorial and remain partly unknown.**

Individual risk cannot be accurately predicted.

→ Risk is therefore assessed at the population level, using:

- Absolute risk (AR)
- Relative risk (RR / hazard ratio)

Risk quantification allows the identification of subgroups to guide appropriate prevention and surveillance strategies.

Multiple risk factors have been identified.

Even moderate risk factors ($RR < 2$) should be systematically assessed, as their accumulation or interaction may influence surveillance strategies.

Importantly, risk factors are not additive but multiplicative, which may lead to an overestimation of individual risk.

Hormonal timing

Earlier age at menarche and later age at menopause may partly explain the increase in breast cancer incidence.

Menarche before age 11:

- Established risk factor ($RR \approx 3$)
- \downarrow RR by $\sim 5\%$ per year of delayed menarche

Late menopause (≥ 55 years):

- ↑ risk by ~3% per year

Age at first full-term pregnancy:

- ~30% reduction in breast cancer risk if before age 20, compared with first full-term pregnancy after age 30

Breastfeeding:

- Minimal protective effect
- Observed only in multiparous women who breastfed for ≥ 12 months

Low-risk breast cancer risk factors (RR < 2)

Hormonal treatments

Oral contraceptives

Menopausal hormone therapy (MHT)

- Not considered major breast cancer risk factors
- Favorable benefit–risk balance

Life style

Sedentarism, obesity, alcohol consumption, smoking
Influencable risk factors

Age

- Primary risk factor
- Age-dependent incidence
- Marked increase from **age 45**

Family history of breast cancer

- Second major risk factor
- Key questions:
 - **How many?**
 - **Who?**
 - **At what age?**
- Both family branches involved (*autosomal dominant transmission of genetic mutations*)

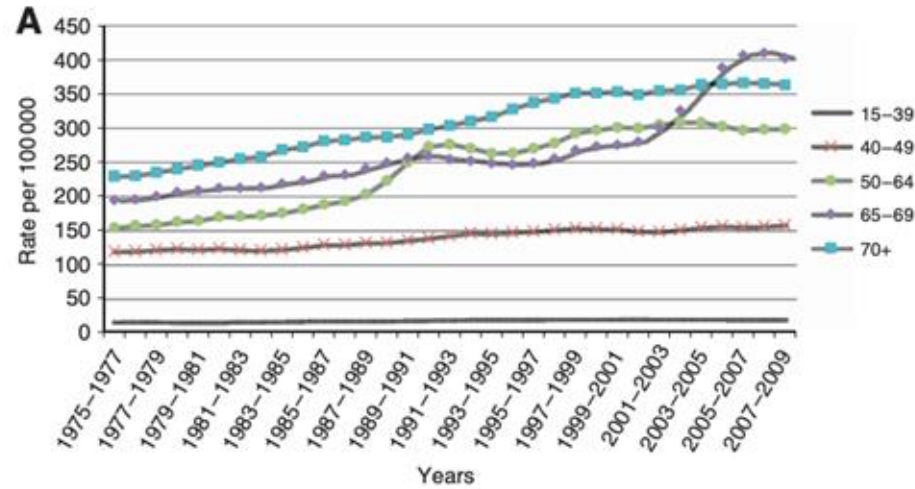
Thoracic irradiation before age 30

- High-risk situation
- Risk level comparable to BRCA1 mutation

Personal history of borderline lesions

- Atypical ductal hyperplasia
- Atypical lobular hyperplasia
- Lobular carcinoma in situ (LCIS)

A single screening strategy cannot be optimal



Evidence from historical randomized trials (1960–1985)

- Systematic mammography every 2–3 years over ~11 years
- Significant reduction in breast cancer mortality

Effect varies with age at screening initiation

- 40–49 years: ~15% mortality reduction
- 50–59 years: ~18% mortality reduction
- 60–69 / 70–74 years: ~32% mortality reduction

Implications

- Most European screening programs are age-based
- Age has historically been used as the primary risk stratification factor

Marmot MG et al The benefits and arms of breaste cancer screening: an independent review. Br J Cancer, 2013;108 (11): 2205-2240



Target population

- Women aged 50–69 years
- Free mammography every 2 years (*two views per breast*)



Excluded populations

- Personal history of breast cancer within the last 10 years
- Genetic or significant familial risk



Age-related extensions (debates)

Women aged 40–49 years

- Incidence already increased
- Unclear benefit within a public health screening program

Women ≥ 70 –74 years

- Insufficient evidence in the literature

Effect of mammographic screening from age 40 on breast cancer mortality

10-year follow-up, randomized controlled trial (*The Age Trial*)

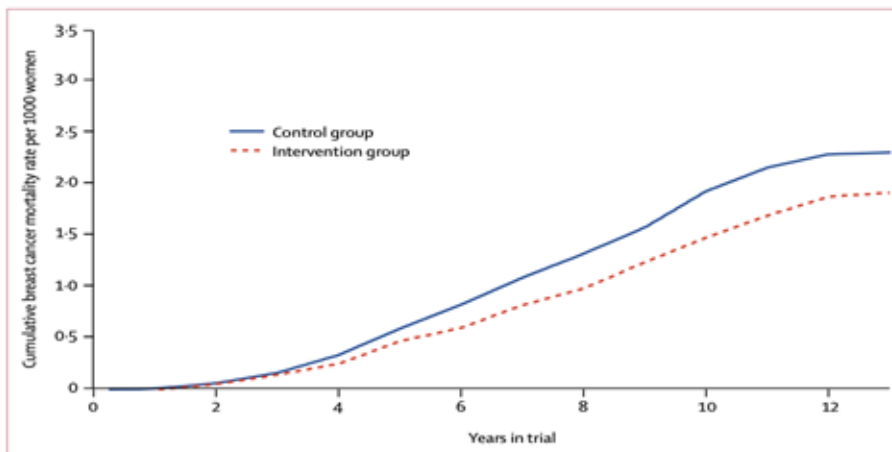


Figure 2: Cumulative breast cancer mortality

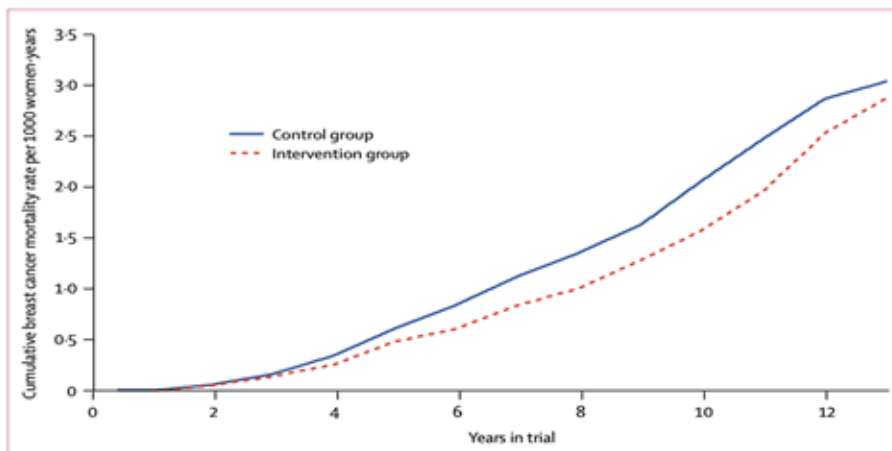


Figure 3: Nelson-Aalen estimate of cumulative breast cancer mortality

Study design

- Randomized controlled trial
- Annual mammography vs no screening before age 50

Population

- 160,921 women
- Aged 39–41 years at inclusion

Main outcome

- No significant reduction in breast cancer mortality at 10 years' follow-up

Sue M Moss; Howard Cuckle; Andy Evans; Louise Johns; Michael Waller; Lynda Bobrow. (2006). *Effect of mammographic screening from age 40 years on breast cancer mortality at 10 years' follow-up: a randomised controlled trial.* , 368(9552), 0–2060.

Table 1 The incidence (per 100 000 person-years) of breast cancer (BC) by screening invitation interval

	Triennial	Annual
Women (n)	7839	6926
Person-years	77 083	68 018
BC cases (n)	111	96
Incidence of BC (per 100 000)	144.0	141.1
RR (95% CI)	Reference	0.98 (0.75, 1.29)

Abbreviations: CI = confidence interval; RR = relative risk. The study with mammography in 1985–2007 in Turku, Finland.

Table 2 All-cause mortality (per 100 000 person-years) and incidence-based^a breast cancer (BC) mortality by screening invitation interval

	Triennial	Annual
Person-years for all-cause mortality	100 738	88 780
Number of deaths (n)	194	205
Total mortality rate (per 100 000)	192.6	230.9
RR (95% CI)	Reference	1.20 (0.99, 1.46)
Person-years for incidence-based breast cancer mortality ^a	100 508	88 543
Number of BC deaths (n)	18	18
BC mortality (per 100 000)	17.9	20.3
RR (95% CI)	Reference	1.14 (0.59, 1.27)

Abbreviations: CI = confidence interval; RR = relative risk. ^aOnly deaths from incident breast cancer diagnosed at ages 40–49 years included. The study with mammography in 1985–2007 in Turku, Finland.

Rationale for annual screening

- Higher incidence of aggressive, fast-growing tumors compared with women aged 50–74
- Higher rate of interval cancers
- Poor prognosis and low survival, independent of stage at diagnosis

Evidence: Finnish study

- Population-based study
- Annual screening from age 40 for women born in even-numbered years
- Every 3 years for women born in odd-numbered years
- 14,765 women included
- 207 breast cancers diagnosed over 10 years
- No difference in incidence or survival observed between screening intervals

Parvinen I, Chiu S, Pylkkänen L, Klemi P, Immonen-Räihä P, Kauhava L, Malila N, Hakama M. Effects of annual vs triennial mammography interval on breast cancer incidence and mortality in ages 40–49 in Finland. Br J Cancer. 2011 Oct 25;105(9):1388–91.

Evidence from Cochrane reviews

- 2001 Cochrane meta-analysis questioned the impact of systematic screening on breast cancer–specific mortality
- Findings confirmed in subsequent reviews (2003, 2011, 2013)

Benefit–harm balance

Among 2,000 women screened annually:

- 1 breast cancer death prevented
- ~200 false-positive results
- ~10 cases of overdiagnosis leading to overtreatment

Overdiagnosis

Diagnosis of a cancer that would not have progressed or affected the patient's lifetime

Main criticisms

- Excessive false positives → unnecessary biopsies and anxiety
- Uncertain prognostic benefit
- Potential risk of radiation-induced cancer

(Olsen et al. 2001; Kösters et al. 2003; Gøtzsche et al. 2011, 2013)

Impact on public trust

- Conflicting messages have contributed to mistrust of organized screening programs

How overdiagnosis is estimated

- Methodological discrepancy
- Estimates rely on mathematical probability models
- Results depend on whether models are correctly adjusted
- Incorrectly adjusted models report overdiagnosis rates of ~40%
- Correctly adjusted models report rates of ~10%

(Raichand et al.)

Raichand S, Dunn AG, Ong MS, Bourgeois FT, Coiera E, Mandl KD. Conclusions in systematic reviews of mammography for breast cancer screening and associations with review design and author characteristics. Syst Rev. 2017 May 22;6(1):105.

False positives

- Breast tomosynthesis is associated with a significant reduction in false-positive recalls
- Approximately 20 fewer false positives per 1,000 women screened

Cancer detection

- Increase in breast cancer detection rate of +1.1 to +1.3 per 1,000 women
- Preferential increase in invasive cancer detection
- No increase in detection of ductal carcinoma in situ (DCIS)

Evidence base

- Consistent findings across multiple studies
- Meta-analysis (BREA): 4 prospective + 7 retrospective trials

Radiation exposure

- Additional radiation from tomosynthesis likely mitigated by the use of synthetic mammography

Study population

- ~19,000 women in England
- Comparison between:
 - Screen-detected breast cancers
 - Symptomatic breast cancers (no prior screening)

Key findings

- Tumors > 2 cm were more than twice as frequent in symptomatic cancers
- Overall survival:
 - 56% in screen-detected cancers
 - 48% in symptomatic cancers

Interpretation

- Screening is associated with detection of smaller tumors
- Screen-detected cancers show a more favorable prognosis

Positive impact of breast cancer screening in detecting smaller tumors

Radiation-related risk

- Breast cancer screening involves low-dose radiation
- Strict quality control minimizes radiation exposure

Population-level evidence

- Large cohort study (1.7 million women)
- For 1 potentially radiation-induced cancer, 156 to 312 breast cancer deaths are prevented

Key message

- The benefit–risk ratio strongly favors screening
- Radiation risk is very low compared with the survival benefit

Warren LM, Dance DR, Young KC. Radiation risk of breast screening in England with digital mammography. Br J Radiol. 2016 Nov;89(1067):20150897.

Comparaison des doses de rayonnements

La **radioactivité** étant présente naturellement, nous y sommes tous exposés chaque jour. **L'exposition moyenne** totale au rayonnement naturel est estimée à **2,4 mSv/an**.

Le tableau ci-dessous compare les doses de radiation de quelques examens d'imagerie médicale avec les doses émises par le fond naturel d'irradiation (rayonnement cosmique, terrestre...)

Par exemple, la dose délivrée, lors d'une radiographie de l'abdomen correspond à la dose du fond naturel d'irradiation reçue pendant une période de trois mois. Lors d'un scanner de l'abdomen, cette période est de quatre ans ou 48 mois. La comparaison des deux examens montre que la dose de radiation d'un scanner de l'abdomen est 16 fois plus élevée que celle d'une radiographie. Ce tableau n'est qu'indicatif : l'évolution des techniques peut modifier ces doses estimées, en général dans le sens d'une diminution.

	Sources du rayonnement	Dose en millisievert	Durée d'exposition naturelle nécessaire pour atteindre la même dose
	Rayonnement naturel en Belgique	2,4 mSv	1 an
Activités de la vie quotidienne	4 heures dans un avion pour passer (en raison de l'altitude plus élevée et de l'atmosphère raréfiée)	0,005 mSv	1 jour
	7 jours de ski en montagne	0,005 mSv	1 jour
Radiographie	Radiographie de la colonne lombaire (examen complet)	1,9 mSv	9 mois
	Radiographie de l'abdomen	0,5 mSv	3 mois
	Radiographie du bassin	0,5 mSv	4 mois
	Mammographie	0,3 mSv	1,5 mois
	Radiographie pulmonaire (vue latérale)	0,06 mSv	9 jours
	Radiographie pulmonaire (vue de face)	0,04 mSv	6 jours
CT-scan	CT-scan angiographique du coeur	10,5 mSv	4,5 ans
	CT-scan de la colonne lombaire	7 mSv	3 ans
	CT-scan de l'abdomen	7 mSv	4 ans
	CT-scan pulmonaire	3 mSv	15 mois

Breast density as a breast cancer risk factor

Key characteristics

- Breast density is multifactorial (genetic, biological, hormonal and lifestyle-related)
- It is an independent and significant risk factor for breast cancer

Clinical implications

- Breast density must be systematically reported on mammography reports
- Women with dense breasts should be clearly informed about the potential benefit of additional screening modalities

Magnitude of risk

- High breast density is associated with an average RR of 4.64

Mac Cormac VA, Dos Santos Silva I et al, Cancer Epidemiol Biomarkers Prev 2006
Cummnngs SR et al: J Natl Cancer Inst, 2009

Breast density: evidence and classification

Epidemiological evidence

- McCormack et al., 2006
RR = 4.64 (95% CI: 3.64–5.91) for density >75%
- Cummings et al., 2009 (meta-analysis)
RR = 4.20 (95% CI: 3.61–4.89) compared with density <25%

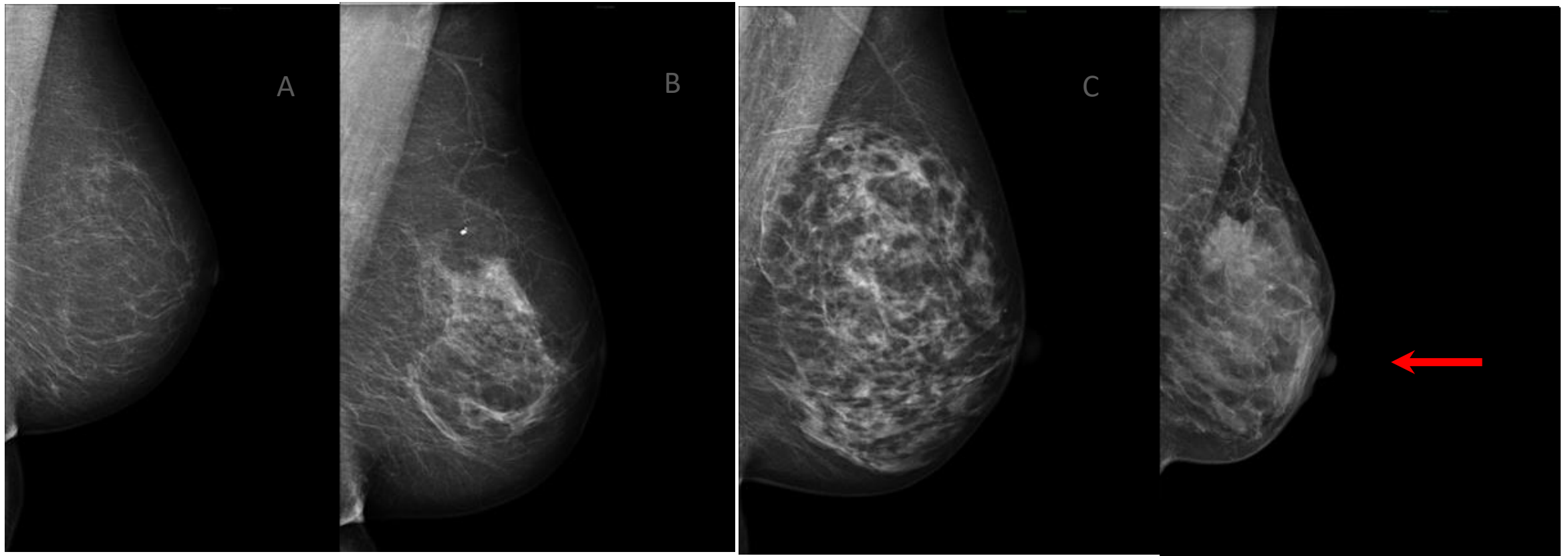
ACR breast density classification

- A: < 25% glandular tissue
- B: 25–50%
- C: 50–75%
- D: > 75%

Clinical relevance

- Increasing density → higher cancer risk
- Increasing density → lower mammographic sensitivity

Mac Cormac VA, Dos Santos Silva I et al ,Cancer Epidemiol Biomarkers Prev 2006
Cummings SR et al: J Natl Cancer Inst, 2009



Almost entirely fatty

Scattered area of
fibroglandular tissue

Heterogeneously dense

Dense

BI-RADS (Breast Imaging Reporting and Data System) classification of breast density of the ACR

Target population

- Women with extremely dense breasts (ACR type D)

Screening strategy

- Annual screening from age 40
- No predefined upper age limit
- Particularly recommended in case of a family history of breast cancer

Role of MRI

- Supplemental breast MRI every 2–3 years for women with extremely dense breasts
- Breast MRI may be used as a stand-alone screening modality in this population

Marcon M, Fuchsjäger MH, Clauser P, Mann RM. ESR Essentials: screening for breast cancer - general recommendations by EUSOBI. Eur Radiol. 2024 Oct;34(10):6348-6357.

Screening in women with extremely dense breasts Recommendations of the European Society of Breast Imaging

•EUSOBI now recommends that women should be appropriately informed about their individual breast density – and on the diagnostic and prognostic implications of having dense breasts – by all (European) organizations that offer breast screening, in order to help them make well-balanced choices.

•EUSOBI now recommends that supplemental screening is recommended in women with extremely dense breasts.

•EUSOBI now recommends that such supplemental screening should be done preferably with MRI, because for the time being, level I evidence is available only for MRI screening. EUSOBI recommends such supplemental MRI screening to be offered to women with extremely dense breasts, from age 50 to 70, and at least every 4 years, preferably every 2 to 3 years. MRI can be used as a stand-alone screening technique (without mammography).

•EUSOBI recommends that, where MRI screening is unavailable for reasons explained below, ultrasound in combination with mammography may be used as an alternative. In these cases, however, EUSOBI recommends informing women adequately about the different performance levels of different non-mammographic screening methods.

•EUSOBI acknowledges the fact that before a population-wide use of non-mammographic screening methods (screening ultrasound and screening breast MRI) is put to practice in women with extremely dense breasts, the necessary quality assurance systems and benchmarks must be established for these non-mammographic screening methods similar to those that are in place for mammographic screening. This will take some time to prepare and to implement; in view of the degree of underdiagnosis associated with pure mammographic screening in women with extremely dense breasts, EUSOBI recommends national societies to act on this now, and with high priority. The EUSOBI guidelines on breast MRI or on screening ultrasound could serve as suitable templates.

•EUSOBI underscores that, even in the absence of national programs that offer MRI screening as part of national healthcare, women should be informed about this recommendation in an unbiased and objective way according to the principle of “shared decision making”.

EUSOBI wishes to underscore that “shared decision making” will likely result in more individualized screening approaches. This may interfere with current measures of effectiveness of screening programs that consider overall participation rates as an important indicator of quality. Of course, demonstrating a reduction of mortality on a population wide level requires high participation rates – but this should not lead to discouraging tools that may not yet be broadly available or acceptable, but can effectively avoid premature death from breast cancer in individual women.



Personal history of high-risk histological lesions

- No prospective randomized studies available
- Evidence mainly derived from retrospective studies with selection bias
- Annual screening strategy, without predefined upper age limit
- Particularly relevant in young women with dense breasts
- According to ACR, annual breast MRI may be considered on a case-by-case basis

Family history of breast cancer

- Annual screening from age 40 in women with a first-degree relative diagnosed after age 45
- Screening should start 5 years before the age at diagnosis in the affected first-degree relative

Oeffinger KC, Fontham ET, Etzioni R, Herzig A, Michaelson JS, Shih YC, Walter LC, Church TR, Flowers CR, LaMonte SJ, Wolf AM, DeSantis C, Lortet-Tieulent J, Andrews K, Manassaram-Baptiste D, Saslow D, Smith RA, Brawley OW, Wender R; American Cancer Society. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. JAMA. 2015 Oct 20;314(15):1599-614

Who?

- Very high genetic risk
- 5-year breast cancer risk > 6%

When & how?

- From age 30
 - Annual breast MRI + mammography
 - Clinical exam every 6 months
- From age 65
 - Return to standard screening
 - Annual mammography only
 - Stop MRI

Why MRI?

- MRI + mammography:
 - +18.3 cancers / 1,000 women
- Compared to:
 - Ultrasound: +2–4 / 1,000
 - Tomosynthesis: +1–2 / 1,000

Practical updates

- Abbreviated MRI
 - < 10 minutes
 - Detection rate comparable to standard MRI
- MRI-only screening
 - Li-Fraumeni syndrome
 - Cowden disease (radiosensitive patients)

From genetics to precision medicine

- **Second decade of the 21st century**
Genetic mutations alone were not sufficient to assess cancer risk.
- **Next step**
Development of large biobanks integrating:
 - Genetic data
 - Biological and radiological factors
- **Precision medicine era**
Supported by major government funding programs (United States, Canada)
- **Core principle**
Personalized screening to:
 - Maximize cancer detection
 - Reduce negative impacts
 - Adapt screening to individual risk

Study design (WISDOM & MyPeBS)

- Two multicenter trials (USA & Europe)
- Women 40–70 years
- very high-risk excluded
- Randomization:
 - Standard screening
 - Risk-based screening
- Risk stratification by saliva test
- 5-year breast cancer risk

Risk-based screening strategy

- Low risk ($RR < 1\%$) → Mammogram every 4 years
- Moderate risk ($RR 1-1.67$) → Mammogram every 2 years ± ultrasound
- High risk ($RR \geq 1.67$ and $< 6\%$) → Annual mammogram ± ultrasound
- Very high risk ($RR > 6\%$) → Annual mammogram + MRI



WISDOM and MyPeBS: Personalized breast cancer screening trials operating in distinct international contexts



K. Leggat Barr¹, P. Giorgi Rossi², M. Guindy³, F. Gilbert⁴, M. Roman⁵, J. Burrión⁶, H. De Koning⁷, S. de Montgolfier⁸, L. Giordano⁹, D. Keatley¹⁰, J. Deleuze¹¹, E. Gauthier¹², S. Michiels¹³, C. Vissac-Sabatier¹⁴, H. Anton-Culver¹⁵, S. Borowsky¹⁶, S. Brain¹⁷, J. Esserman¹⁸, E. Ziv¹⁹, A. Fiscali²⁰, D. Goodman-Gruen²¹, D. Heditsian²², R. Hatt²³, V. Lee²⁴, D. Moorehead²⁵, A. Nalew²⁶, O. Olopade²⁷, H. Park²⁸, B. Parker²⁹, A. Petruse³⁰, M. Scheuner³¹, L. van 't Veer³², V. Arasu³³, M. Eklund³⁴, L. Madlensky³⁵, Y. Shieh³⁶, N. Wenger³⁷, J. Tice³⁸, C. Kaplan³⁹, A. Kaster⁴⁰, R. Lancaster⁴¹, A. LaCroix⁴², S. Delaloge⁴³, L. Esserman⁴⁴

1. University of California, San Francisco; 2. University of California, San Francisco; 3. University of California, San Francisco; 4. University of California, San Francisco; 5. University of California, San Francisco; 6. University of California, San Francisco; 7. University of California, San Francisco; 8. University of California, San Francisco; 9. University of California, San Francisco; 10. University of California, San Francisco; 11. University of California, San Francisco; 12. University of California, San Francisco; 13. University of California, San Francisco; 14. University of California, San Francisco; 15. University of California, San Francisco; 16. University of California, San Francisco; 17. University of California, San Francisco; 18. University of California, San Francisco; 19. University of California, San Francisco; 20. University of California, San Francisco; 21. University of California, San Francisco; 22. University of California, San Francisco; 23. University of California, San Francisco; 24. University of California, San Francisco; 25. University of California, San Francisco; 26. University of California, San Francisco; 27. University of California, San Francisco; 28. University of California, San Francisco; 29. University of California, San Francisco; 30. University of California, San Francisco; 31. University of California, San Francisco; 32. University of California, San Francisco; 33. University of California, San Francisco; 34. University of California, San Francisco; 35. University of California, San Francisco; 36. University of California, San Francisco; 37. University of California, San Francisco; 38. University of California, San Francisco; 39. University of California, San Francisco; 40. University of California, San Francisco; 41. University of California, San Francisco; 42. University of California, San Francisco; 43. University of California, San Francisco; 44. University of California, San Francisco

Background on the WISDOM & MyPeBS trials

- WHAT:** WISDOM (Women Informed to Screen Depending on Measures of risk) (NCT02620852) & MyPeBS (My Personal Breast Screening) (NCT03672331) are two prominent risk-based breast cancer screening (RBS) trials based in the US and Europe & Israel, respectively.
- SIMILAR TRIAL AIMS:** Both trials aim to assess whether:
 - RBS is as safe as current screening (no increase incidence of stage> II/III breast cancers)
 - Enhance resources to those who are high risk, while minimizing harm to those at lowest risk
- TRIAL ENROLLMENT:** WISDOM (2016-2023; 46,289 women) vs. MyPeBS (2019-2025; 53,143 women)
- RECRUITMENT STRATEGIES:**
 - Eligibility between the two trials were similar, (40-74 vs 40-70) & no prior breast cancer history
 - Both are randomized 1:1 to RBS vs. country-based standard of care screening (WISDOM had a pragmatic option).

Risk Assessment & Screening Assignments in both trials

	WISDOM	MyPeBS
RISK ASSESSMENT		
BCSC (version 2)	Yes	Yes
PRS (up to 313 SNPs)	Yes	Yes
9 gene panel of breast cancer susceptibility genes	Yes	Yes
SCREENING ASSIGNMENT		
Highest Risk	Some 18 months, alternating with Mammogram & MRI	Some 18 months, alternating with Mammogram & MRI
Elevated Risk	Same, every year	Same, every year
Lowest risk	2 year for no screen and 3 risk + average 10-year-out	4 year
Control	1 year	2 year
Screening starting age	40	40
SCREENING GUIDELINES	Annual (ACR, NCCN) to biennial screening @ 40 (USPSTF)	2 yrs in France, Belgium, Italy, Spain, Israel) to 3 yrs in the UK @ 50

Table 1: Comparison of MyPeBS & WISDOM Risk Assessment & Screening Assignments

The WISDOM Study is sponsored by the Patient Center Outcomes Research Institute (PCORI) and the National Cancer Institute (NCI), and the Department of Defense. The MyPeBS study is funded by the Department of Defense.

Results – Risk Distribution in WISDOM & MyPeBS

Figure 1: WISDOM Risk Assessment & Stratification in the Risk-based WISDOM cohort



Figure 2: MyPeBS Risk Assessment & Stratification in the MyPeBS cohort

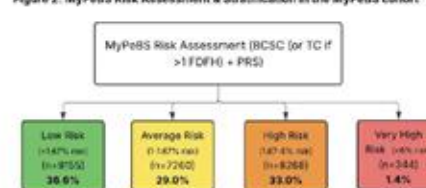
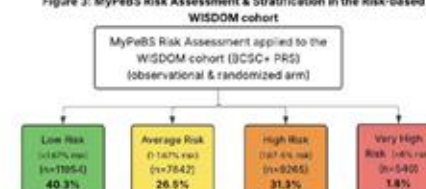


Figure 3: MyPeBS Risk Assessment & Stratification in the Risk-based WISDOM cohort



Legend:

BCSC: Breast Cancer Surveillance Consortium version 2 5-year risk

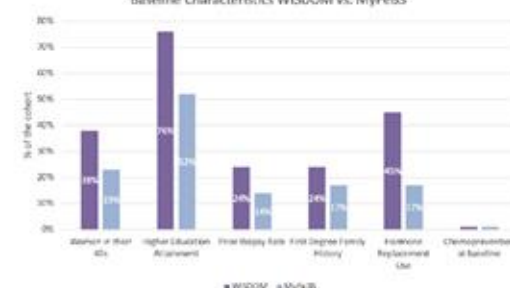
PRS: Polygenic Risk Score (up to 313 SNPs)

TC: Tyrer Cuzick 5-year risk assessment

FDRH: First Degree Family History

Results – Baseline Demographics

Baseline Characteristics WISDOM vs. MyPeBS



- Baseline risk demographics were slightly different, evidenced above.
- Median age was similar (54 vs. 55).
- Baseline BMI was higher in WISDOM (27.6 vs 25.3).

Conclusion

- The risk distribution between the two trials are very similar.
- Baseline characteristics were slightly different, especially in prior biopsy rates and hormone replacement use.
- Screening schemes are also similar, except for low-risk women (every 2 yrs (WISDOM) vs. every 4 yrs (MyPeBS)).
- While the risk distribution using standard cutoffs were similar across trials, the two studies classified risk (i.e. elevated/low) very differently. This provides an exciting opportunity to learn.
- Data emerging from both trials should be generalizable and have the potential to be practice-changing.

Join the WISDOM Study

Join the WISDOM Study and invite your friends and family!

- Enroll in WISDOM at our website – www.thewisdomstudy.org
- Phone: 855-729-2844
- Email: info@wisdomstudy.org

This presentation is the intellectual property of the WISDOM & MyPeBS Study. Contact us at wisdom@pcori.org and mypebs@pcori.org for permission to reprint and/or distribute.

Thank you for your attention