# Update on Swedish High Risk/Personalised Screening

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BREASTSCREEN AUSTRALIA CONFERENCE 2024

TOWARDS TOMORROW

INCLUSION · EVIDENCE · SHOWCASE · CHANGE

National Convention Centre Canberra · 13 - 15 March 2024

REGIONALA CANCERCENTRUM I SAMVERKAN

# Bröstcancer

Nationellt vårdprogram

Recommendations for previously cancer-free individuals at highly increased risk (includes carriers of pathogenic variants in *BRCA1, BRCA2* and *PALB2*:

Annual imaging (breast) from 25 to approximately 74 years of age, including breast MRI up to approximately 55 years of age (strong scientific evidence ++++)

REGIONALA CANCERCENTRUM I SAMVERKAN

# Bröstcancer

## Nationellt vårdprogram

Recommendations for moderately increased risk (based on the presence of pathogenic variant associated with moderately increased risk, alternatively women with an epidemiologically based greater than 20% lifetime risk)

- Annual diagnostic imaging (breast) from approximately 5 years before the case in the family or from the age of 40 to 60 (very low certainty of the evidence +).
- For follow-up before the age of 50 and in the case of mammographically dense breasts, one can, for increased sensitivity, supplement with, for example, ultrasound (low certainty of the evidence for the additional benefit of ultrasound to mammography screening ++).

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# Bröstcancer

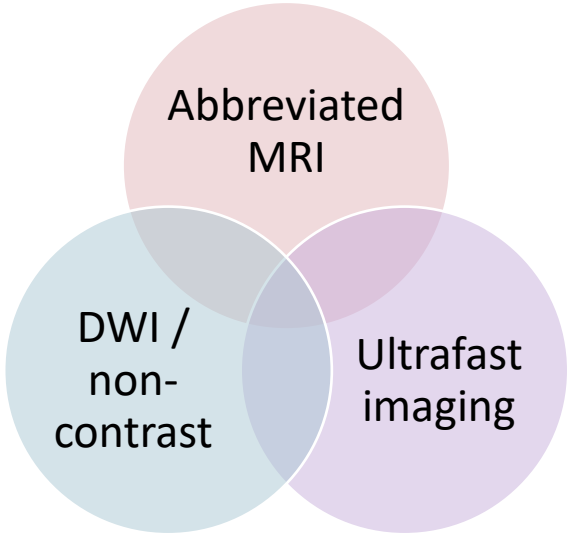
## Nationellt vårdprogram

Recommendations for slightly increased risk
(based on epidemiological risk assessment, corresponding to up to 20% lifetime risk)

- Mammography screening in the service screening program (strong certainty of the evidence ++++) for reduced breast cancer-specific mortality in women who are invited to mammography screening).

# Evidence MRI high risk

- Mortality data largely missing
- Stage migration by early detection is beneficial
- Rates of interval cancers reduced by 50%

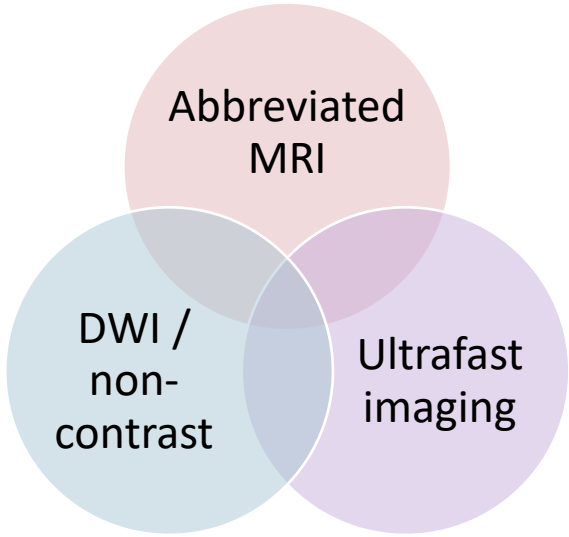



Evans DG. *Cancer Heredit Cancer Clin Pract* 2016

Vreemann S. *Radiology* 2018

# Evidence for MRI screening

- MR imaging screening generally deemed cost-effective for *BRCA* carriers
  - Adherence high among carriers confirmed by genetic testing (80%–90%)
  - MR imaging screening has the potential to become more cost-effective than mammography over time



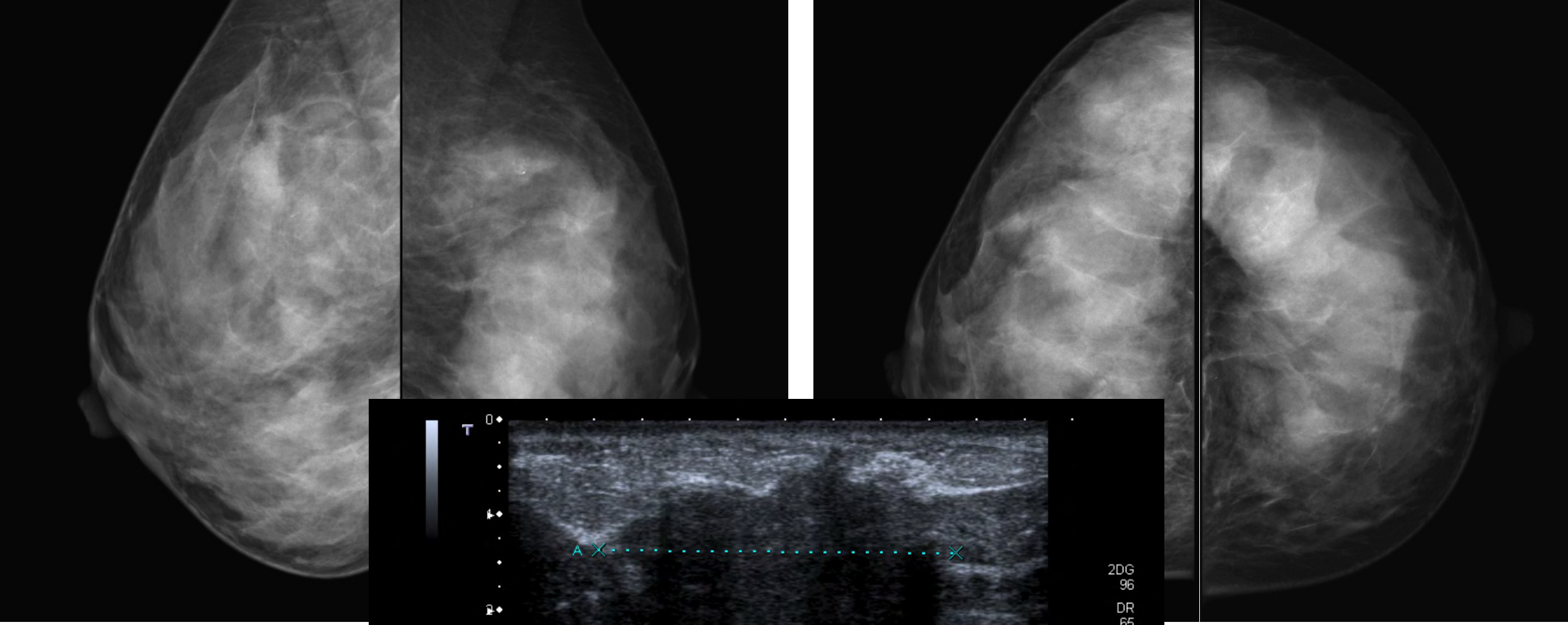

Mann RM *Invest Radiol* 2014

# Supplemental mammography

- Sensitivity of mammography is 25 – 59% in higher risk women
- Higher risk women more likely to be diagnosed with larger, node positive malignancies on screening mammography and higher interval cancer rates.
- Value of concurrent mammography in younger high-risk women undergoing MRI screening - may benefit from reduced radiation dose by forgoing mammography?

Sardanelli F *Investigative Radiology* 2011

Robson M *New England Journal of Medicine* 2007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# Supplemental mammography

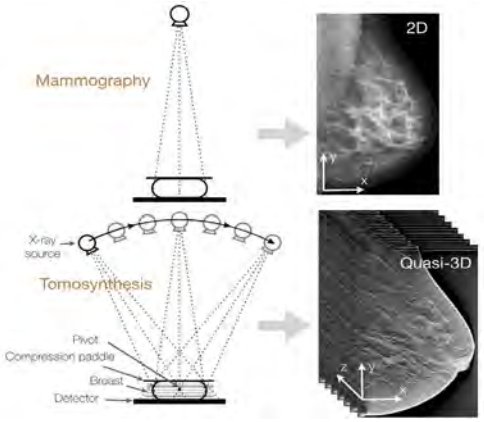
- Evidence to suggest mammography only adds a small amount of increased cancer detection in BRCA1 carriers under 40 if MRI used regularly

- Study *BRCA1/2* mutation carriers of all ages (BRCA1=1219 and BRCA2=732)
  - Adding mammography to MRI did not significantly increase screening sensitivity
  - However, in women with *BRCA2* mutation younger than 40 years, one-third of breast cancers were detected by mammography only

Phi X *British Journal of Cancer*. 2016

Heijnsdijk E *Cancer Epidemiology Biomarkers & Prevention*. 2012

# Supplemental DBT




- DBT detects more cancers and decreases false positive recalls compared with DM alone especially young, dense breasts - do higher risk women benefit from DBT?

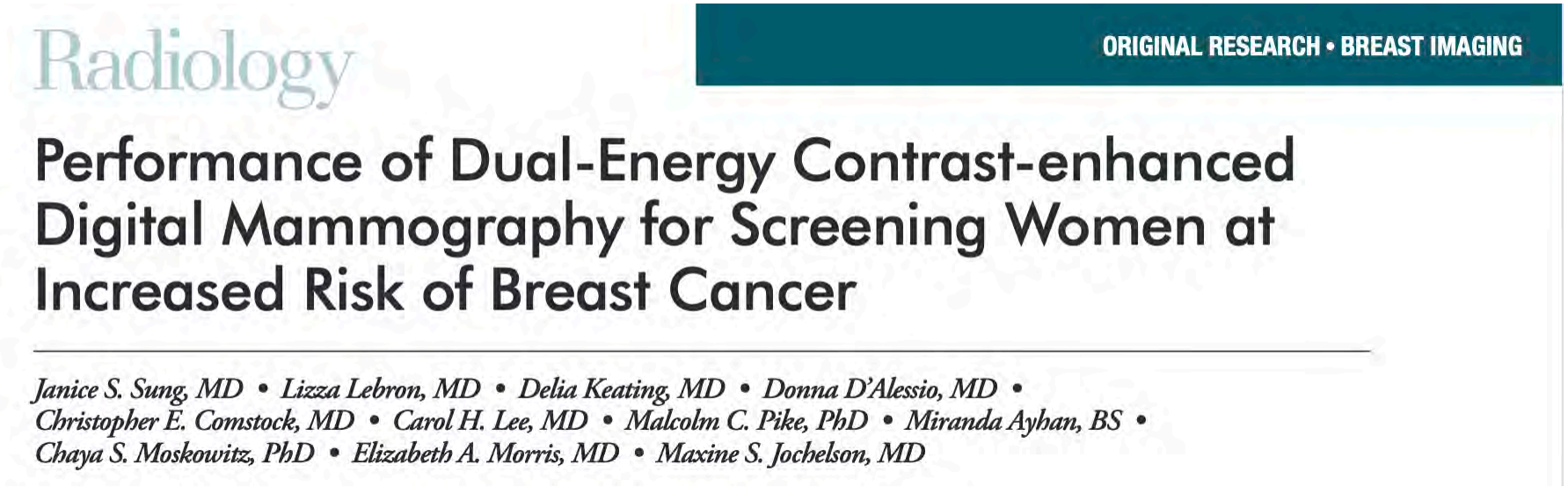
- Limited data on DBT in HR. Effects of DM and DBT similar to average risk women

- Study 4418 screening MRI following a negative DBT or a negative DM
  - No difference incremental cancer detection rates between the 2 groups

Guidelines from most specialty societies do not clearly mention for or against the use of DBT as a screening modality for women at high risk

Vreemann S *Breast Cancer Res* 2018
Lo G, *Radiology* 2017
Roark AA. *AJR Am J Roentgenol* 2019

# Supplemental CEM




- 100/904 CEM examinations (11.1%), 82 of them *BRCA* mutation carriers (9.1%)

***'Screening CEM may also be beneficial in women at high risk for breast cancer'***

Sung *Radiology* 2019

# Supplemental CEM

- CEM-based breast cancer screening of high-risk women when MRI unavailable or when a woman has major contraindications to MRI
- Stagger CEM and MRI 6 monthly instead of mammography
- Specific indication for CEM for previously irradiated women who have a higher incidence of DCIS that may be missed at MRI

Sung *Radiology* 2019
Cozzi *Quant Imaging Med surg* 2019

# Supplemental US

US finds more cancers

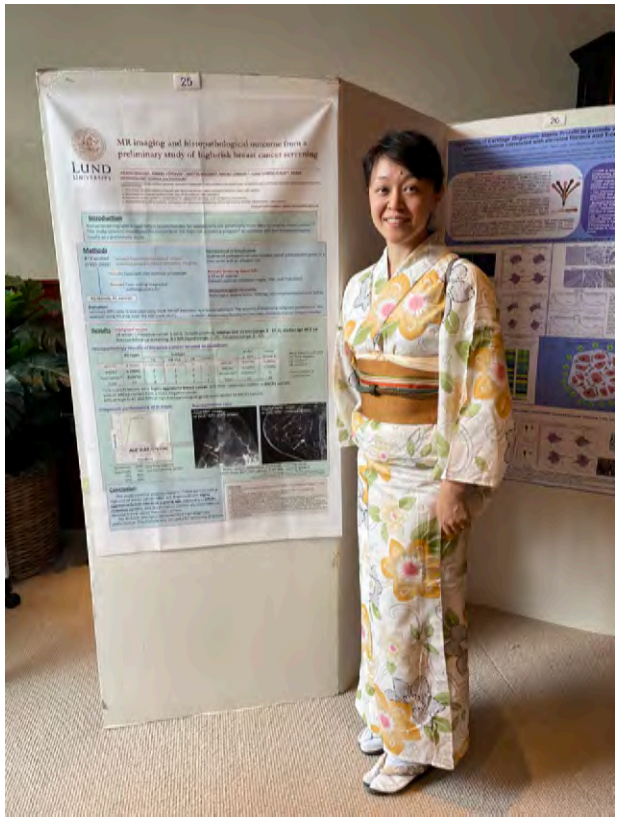
- ACRIN 6666 (prospective multicentre study) women at increased risk
- Supplemental cancer detection rate of 4.3 per 1000
- Cancers found were small, and node negative

**BUT….**

- Labour intensive and increase false positive findings
- Short term follow up recommended at undesirably high rate
- No incremental yield when MRI performed

Some specialty societies recommend screening ultrasound only for high-risk women who qualify, but cannot undergo breast MRI

# Ongoing projects in Region Skåne




**Women's experiences of high risk annual screening with MRI in Sweden**

Ann-Sofi Sjökvist
Radiographer (MRI)
PhD student

**Evaluation of high-risk screening for breast cancer in the south Swedish health care region**

Akane Ohashi, MD PhD
Post doc

# Women's experiences of high risk annual screening with MRI in Sweden

- to describe women's perceptions of inclusion and participation in annual surveillance with MRI (phenomenography)
- to describe women's perceptions of the care relating to breast MRI (phenomenography)
- to shed light on women's experiences and lived experiences (phenomenology)
- to examine person-reported outcome measures (PROs) in women participating annual surveillance with MRI (prospective longitudinal observational study)
- to investigate predictors of affected PRO:s among women participating in annual magnetic resonance imaging breast health screening (prospective longitudinal observational study)

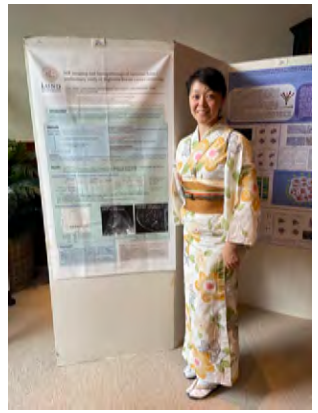

# Perceptions of surveillance with MRI among women with a hereditary risk of breast cancer

| Descriptive categories | Perceptions |
|---|---|
| **Considering own risk of developing breast cancer** | Comprehending own risk based on family narratives<br><br>Appraising own benefits of surveillance |
| **Entrusting oneself to surveillance** | Handing over management<br><br>Dealing with practical issues and diverse emotions in relation to MRI |
| **Living in a cycle** | Planning life hand in hand with surveillance<br>Struggling with fluctuating emotions<br>Questioning own identity |

Ann-Sofi Sjöqvist, Annette Holst-Hansson, Sophia Zackrisson, Jenny Gårdling, Anetta Bolejko

*Journal of Advanced Nursing. Jan 2024*

# Evaluation of high-risk screening for breast cancer in the south Swedish health care region



- Retrospective evaluation of imaging, clinical, demographic, and socio-economic data from the south Sweden high-risk breast cancer screening program to understand the current situation and to enable better personalized screening recommendations, with the following aims:

1) **Identify minimal reliable screening approach**: Analyze the clinical accuracy (sensitivity, specificity, and recall rate) to understanding the screening performance. Evaluation of individual screening methods according to women's background information, as imaging, genetics, and personal and family history of breast cancer.

2) **Examine the long-term outcomes of the screening program**, particularly recurrence-free survival rate, mortality rate, and interval cancers.

3) **Analysis the effect of adherence differences (socioeconomic, educational, and ethnic)** on the participation and outcomes of the high-risk screening program, and suggest potential improvement.

**Akane Ohashi**, Daniel Förnvik, Anetta Bolejko, Niklas Loman, Hans Ehrencrona, Karin Henriksson, Sophia Zackrisson

**848 women**

Women who were included in high-risk screening in 1995-2022

**220 women**

**Exclusion**

164 Family history (no mutation)

28 Mutation but intermediate risk (*ATM, CHEK2, EPCAM, CDH1, NF1*)

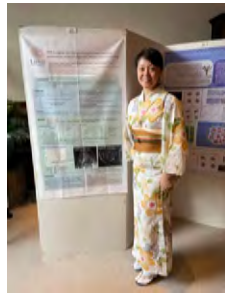
23 Lack of information

5 No screening images

**628 women**

| | Total | Screening | Surveillance |
|---|---|---|---|
| Total Women | 628 | 458 | 170 |
| Screening detected cancer | 37 | 26 | 11 |
| Interval Cancer | 13 | 8 | 5 |
| Mastectomy detected Cancer | 29 | 23 | 6 |
| Total Cancer | 79 | 57 | 22 |

Work in progress. Ohashi et al.



Women who started screening between 1995/10 to 2011/5
MRI performed at least once at screening round
147 women, 149 lesions*

Exclusion:

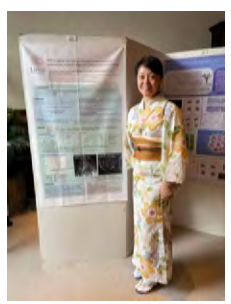
31 women without any Interventional procedure performed
(Still ongoing screening, finalize screening without any intervention etc.)

13 lesions with no MRI before the intervention
5 lesions with no mammography before the intervention

2 lesions with insufficient information

Total
98 women (98 lesions) - 20 cancers

Inclusion: cases in which all three modalities were performed prior to intervention



Work in progress. Ohashi *et al.*

98 women (average age 38 years, range 20-65 years)

| | BRCA1 | BRCA2 | TP53 | Family | Total |
|---|---|---|---|---|---|
| Number | 59 | 23 | 1 | 15 | 98 |

20 breast cancers

| | IDC | ILC | DCIS | Total |
|---|---|---|---|---|
| Number | 13 | 3 | 4 | 20 |

Six (30%, 6/20) cancers were detected by MRI alone

Work in progress. Ohashi *et al.*

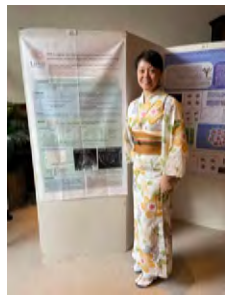
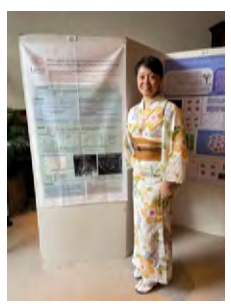


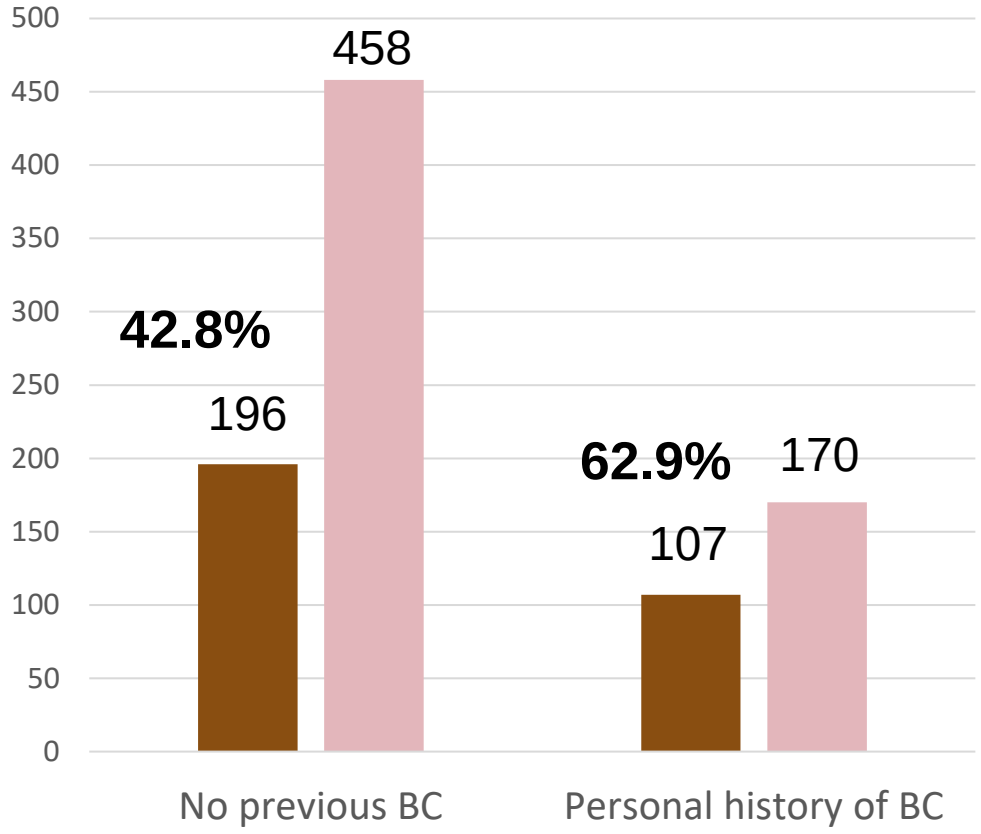
Table 1) Diagnostic performance (sensitivity/specificity)

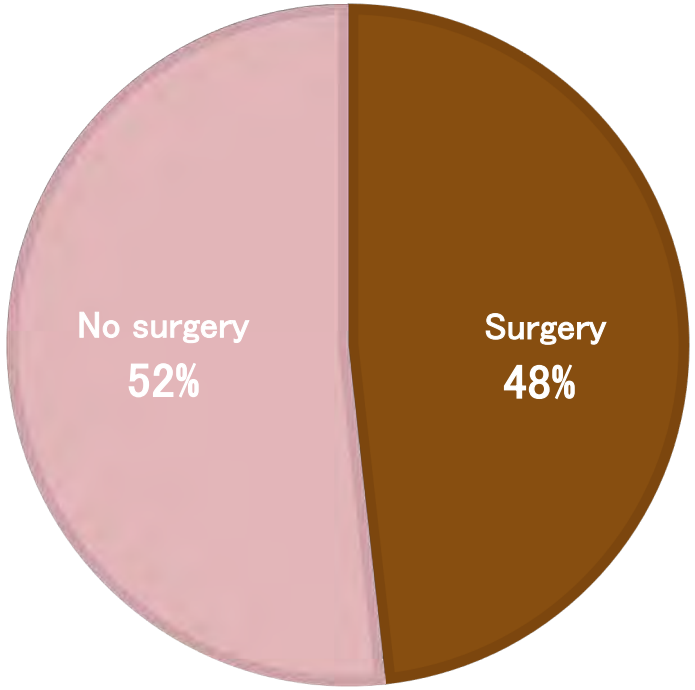
| | Sensitivity | Specificity |
|---|---|---|
| MRI | 80 | 84 |
| MG | 45 | 91 |
| US | 25 | 95 |
| MRI and MG | 85 | 84 |

Work in progress. Ohashi *et al.*



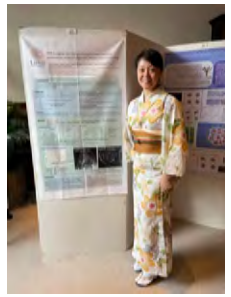
# Prophylactic mastectomy




Cancer 23 Cases 6 Cases

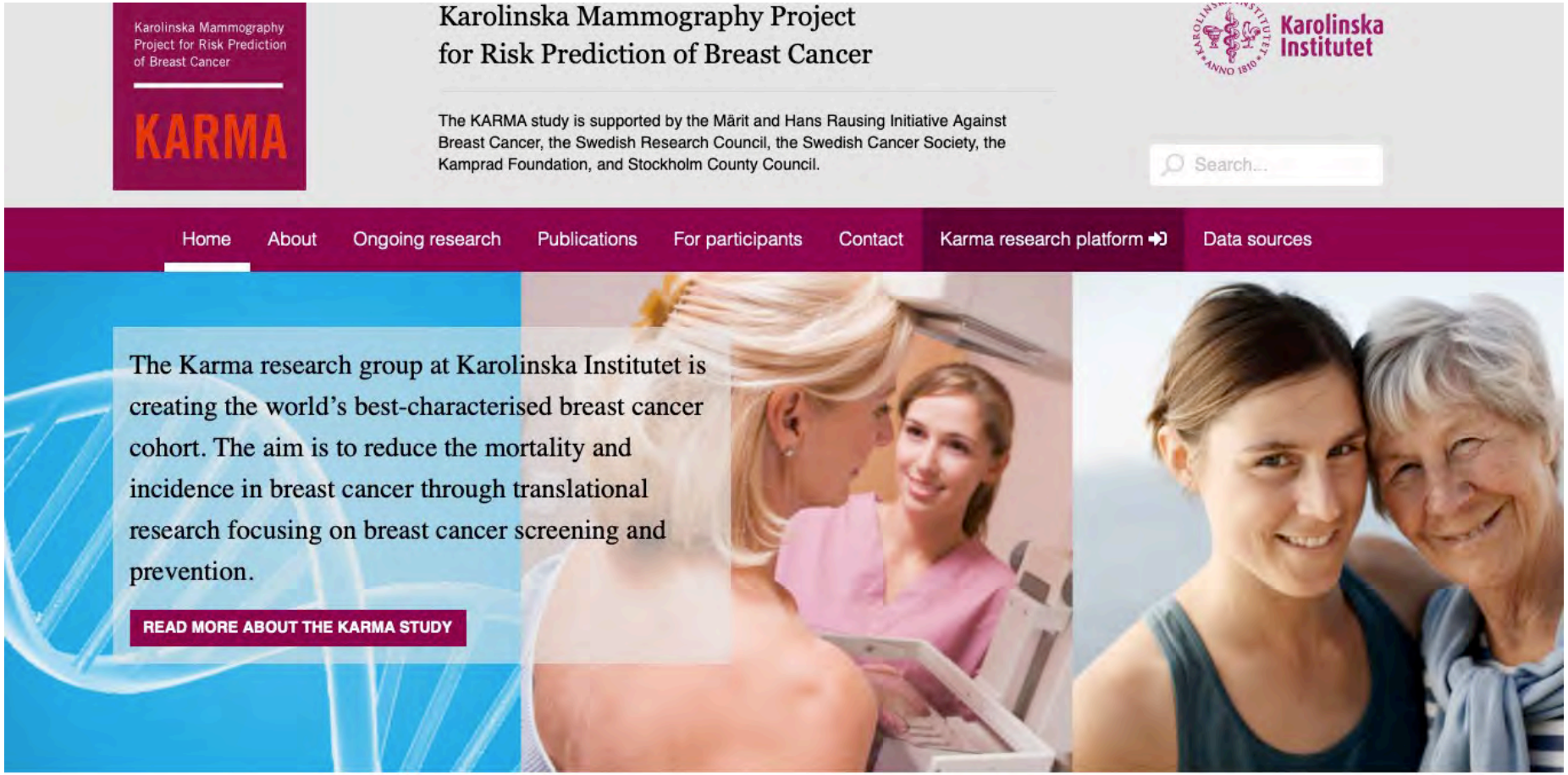
Work in progress. Ohashi *et al.*



# Personalised screening in Sweden?

- Image based risk prediction!

# Personalized screening in Sweden?



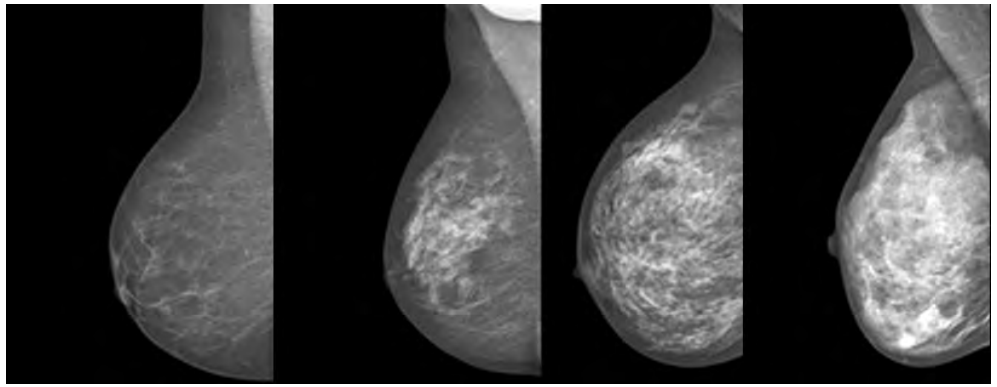

- >70,000 women inluded
- Online questionnaire
- Blood samples (98%)
- 20,000 genotyped

PI: Professor Per Hall

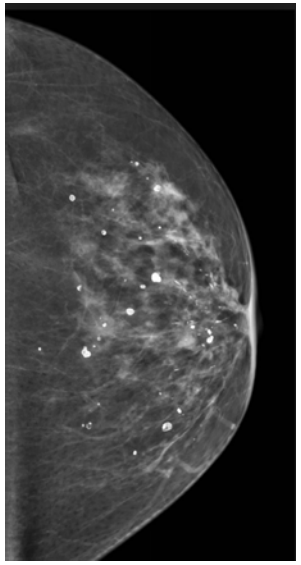
## Stratus 2-year risk model

The risk model should answer the question; *who are the women that will come back with a breast cancer within 2 years of a negative screening mammogram?*

Mammographic density [asymmetry]



Calcifications/masses [asymmetry]



In addition:

- BMI, age, menopausal status, family history, hormone replacement therapy, alcohol, tobacco
- Polygenic risk score (313 SNPs)

# Stratus 2-year risk model

| Model | Risk |
|---|---|
| *KARMA10K cohort (N=1000 cancers)* | |
| 1. Mammographic features + age | **0.72** |
| 2. Model 1 + additional lifestyle + familial factors | **0.73** |
| 3. Model 2 + polygenic risk score | **0.75** |
| *External cohort* | |
| TomoZ, tested with model 1 (N=88 cancers) | **0.71** |
| *Other model performances in KARMA10K* | |
| Polygenic risk score only | **0.65** |
| Tyrer-Cuzick | **0.63** |
| Gail | **0.55** |

*Eriksson, Radiology 2018*

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE 2022

CANCER

# A risk model for digital breast tomosynthesis to predict breast cancer and guide clinical care

Mikael Eriksson[1]*, Stamatia Destounis[2], Kamila Czene[1], Andrew Zeiberg[3], Robert Day[4], Emily F. Conant[5], Kathy Schilling[6], Per Hall[1,7]

Karolinska Institutet

**805 incident breast cancers and a random sample of 5173 healthy women matched on year of study entry in a nested case-control study from 154,200 multiethnic women, aged 35 to 74, attending DBT screening in the United States between 2014 and 2019**

The model included the average of mammographic densities from left and right breasts.
The model also included three scores each for microcalcifications and masses

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

2022

CANCER

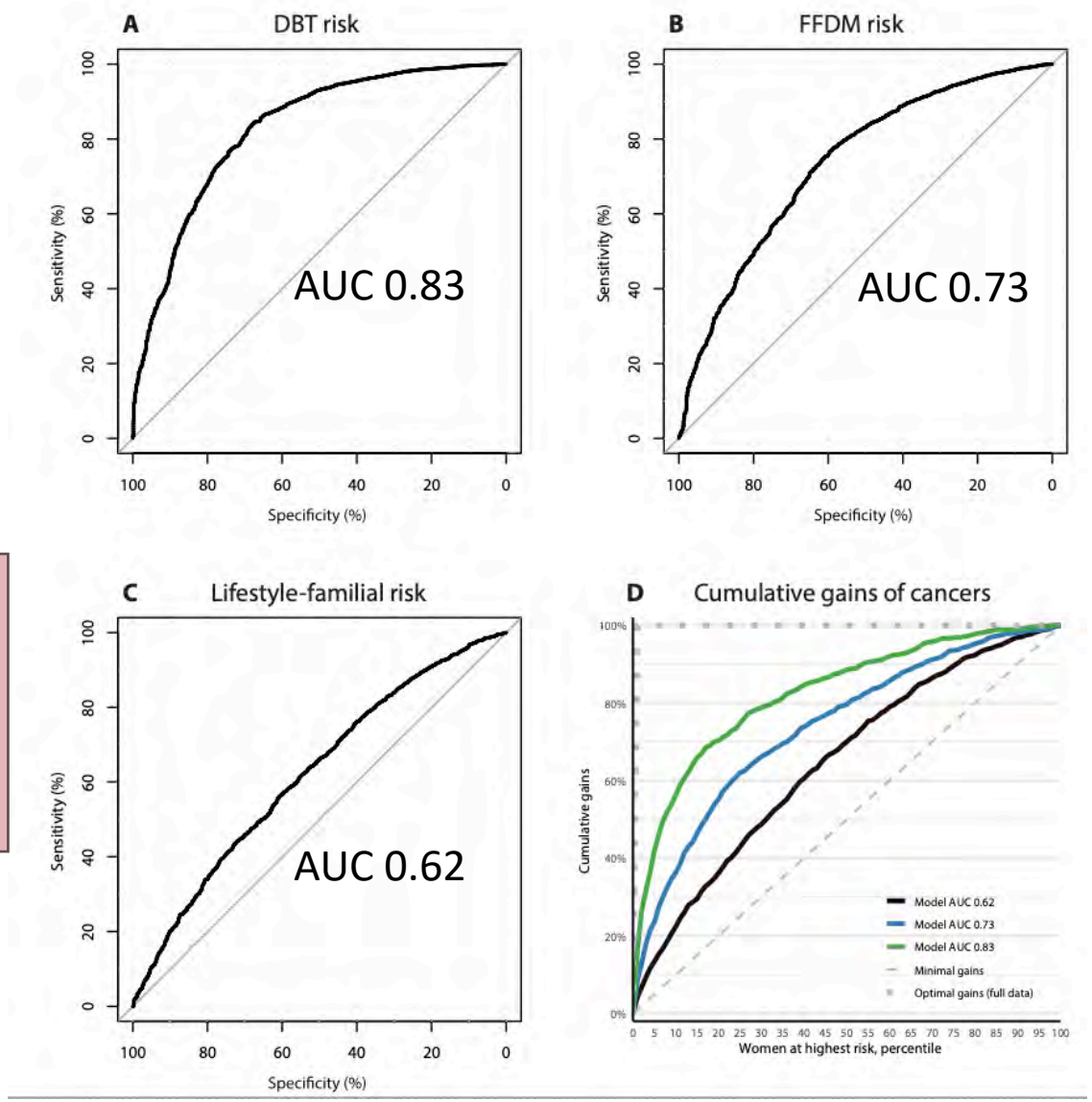
# A risk model for digital breast tomosynthesis to predict breast cancer and guide clinical care

Mikael Eriksson[1]*, Stamatia Destounis[2], Kamila Czene[1], Andrew Zeiberg[3], Robert Day[4], Emily F. Conant[5], Kathy Schilling[6], Per Hall[1,7]

Karolinska Institutet

Simulation studies
2-year risk assessment

If 12% of the women at highest risk had been offered supplemental screening, then potentially up to 59% of the cancers may have been detected with the DBT model compared with 39 and 24% of the cancers using the FFDM- and lifestyle-family–based risk models, respectively.



# Malmö Breast Imaging Database (M-BIG)

**The Malmö Breast Tomosynthesis Screening Trial (2010-15)**

N=14.848 digital mammograms (raw and processed)
N=14.848 digital breast tomosynthesis volumes (raw and processed)
Double reading data with malignancy scoring for all images
N= 139 screening detected breast cancers
N=22 interval cancers
3-year follow-up

**Reference screening population (2010-15)**

N=96.037 screening events
N= 540 cancers
N= 188 interval cancers

**Mammography and digital breast tomosynthesis exams (2004-9 and 2016-18)**

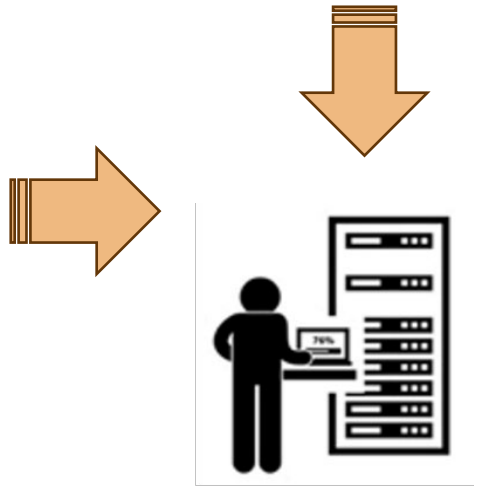
N=approx. 300.000 screening events
N= approx. 5000 digital breast tomosynthesis volumes (clinical)
N= cancers?

# Register data and biobank

Regional Tumor Register

INCA (Quality Register Breast Cancer)

Sweden Cancerome Analysis Network
Breast : Genomic Profiling of Breast Cancer (SCAN-B)



Dahlblom V, Dustler M, Bolejko A, Bakic P, Granberg H, Johnson K, Lång K, Förnvik K , Tingberg A, Zackrisson S.
The Malmö Breast ImaginG (M-BIG) Database: Objectives and Development. *J Med Imaging 2023*

# Risk prediction model development M-BIG

Link transcriptomics data and mammographic data by the linkage of M-BIG and the SCAN-B cohorts

- Identify underlying molecular features of pre-defined mammography tumor image categories (screening detected vs clinically detected tumors, mass vs spiculated tumors)

- Discovery-based analyses of global gene expression data in relation to image-based data

- Artificial intelligence supported, image-based risk prediction models will be developed

**Malmö Breast ImaginG database: objectives and development**

Victor Dahlblom[a,b,*] Magnus Dustler[a,c] Anetta Bolejko[a,b] Predrag R. Bakic[a,c] Henrik Granberg[b] Kristin Johnson[a,b] Daniel Förnvik[c,d] Kristina Lång[a,e] Anders Tingberg[c,d] and Sophia Zackrisson[a,b]

*J Med Imaging 2023*

# Conclusions

- MRI screening increases cancer detection rate in high-risk women
- Supplemental imaging adds relatively little to the high sensitivity of MRI

➢High risk screening in Sweden: MRI, mammography, (US)

➢Personalized screening is under investigation

➢Image-based risk prediction models promising for short-term risk assessment

- Professor Per Hall, Karolinska institutet, Stockholm
- Dr Fleur Kilburn-Toppins, Consultant Breast Radiologist Cambridge University Hospital, UK

# Lund University breast Cancer Imaging Group, LUCI

Department of Translational Medicine

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Pontus Timberg MSc, PhD

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Hanna Tomic, MSc, PhD candidate

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Nadia Chaudry, MD, PhD candidate

Jakob Olinder, MD, PhD candidate

REGIONALA CANCERCENTRUM I SAMVERKAN

Allmänna Sjukhusets i Malmö Stiftelse för bekämpande av cancer

Mats Paulssonstiftelserna

Knut och Alice Wallenbergs

CANCERFONDEN

Stiftelsen för cancerforskning vid Onkologiska kliniken vid Universitetssjukhuset MAS

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