

# ***Non-progressive breast carcinomas detected at mammography screening: a population study***

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# Background

- **Breast cancer develops gradually;**  
From early stages to clinical symptomatic breast cancer
- **Mammography screenings** *aims* to reduce mortality by;  
**Earlier detection** => earlier treatment => better prognosis
- Challenge:

Do all preclinical carcinomas have a potential for progressing to clinical disease?

(by time if the women do not die of some other cause)

# Balancing mammography screening

- “to screen or not to screening”

- **Reduced breast cancer mortality**
- Less invasive treatment?



- **Overdiagnosics**
- **Overtreatment**

- Cost
- Re-calls / fear
- Time use for screening

Which age groups should be screened?  
How often should we screening?  
... **it's a balance of pros an cons**

The key question:

*What is the natural progression  
of screening detected tumors?*

Since almost all screening detected cancers are treated  
we can not directly observe its progression 🤔

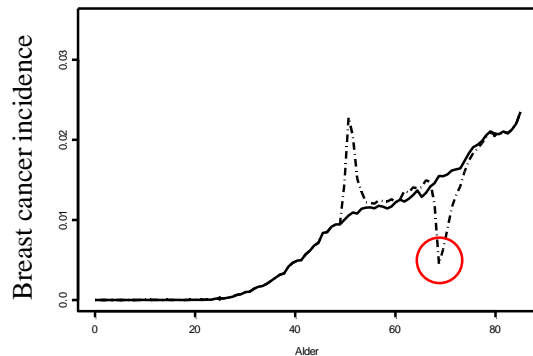
Using “hidden” data:

Would non-progressive leave  
some signs (“tracks”) in our data?



# Indicators of non-progressive tumors in population data

- Breast cancer **incidence increases when initialing screening**
- **If all tumors progress we will see a full compensation fall** in incidence when people leave the screening program due to high age



Simulation of screening  
50-69 years of age, with  
only progressive tumors

- If some do not progress will we see a smaller compensation fall

# Data:

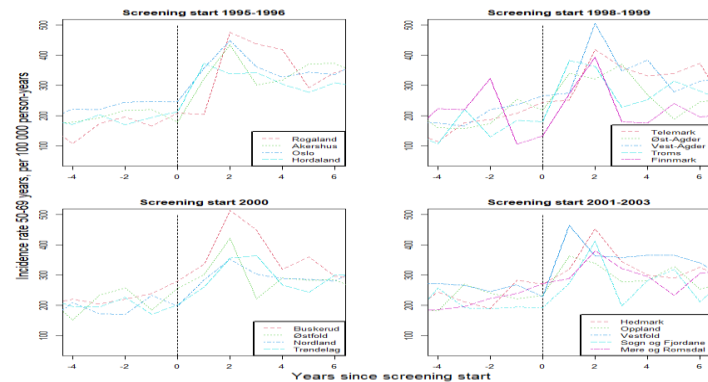
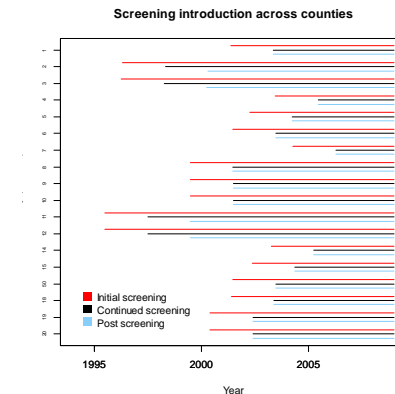
- BreastScreen Norway:  
National public mammography screening program introduced 1995-2005 for women 50-69 years of age
- Data from the Cancer Registry of Norway  
on all Norwegian women 49-85 years of age in 1987-2019.
  - > With mandatory independently reporting from clinicians, pathologists and death certificates
  - > High quality; Only 0.3 % of reported breast cancer cases are based on death certificate only

Remark: We have include both invasive breast cancer and ductal carcinoma in situ [DCIS], as DCIS treatment might stop development of invasive cancers (So any separate analysis would be biased)

# Data structure

Screening was gradually introduced across Norway:

- Giving us lots of comparison groups
- ... and quite complex data to analyze



# Statistical modeling

- *We modeled variations in breast carcinoma incidence when introducing screening*
  - > Adjusted for effects of age, period, birth cohort, county and country wise use of hormone treatment.
- Using an Age-Period-Cohort *Poisson regression* model
  - > with special indicators for the different phases of the screening program and hormone treatment use
  - > and smoothing splines to limited the number of parameters

# For details; See scientific publication

## “ Non-progressive breast carcinomas detected at mammography screening: a population study”

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<https://breast-cancer-research.biomedcentral.com/articles/10.1186/s13058-023-01682-9>

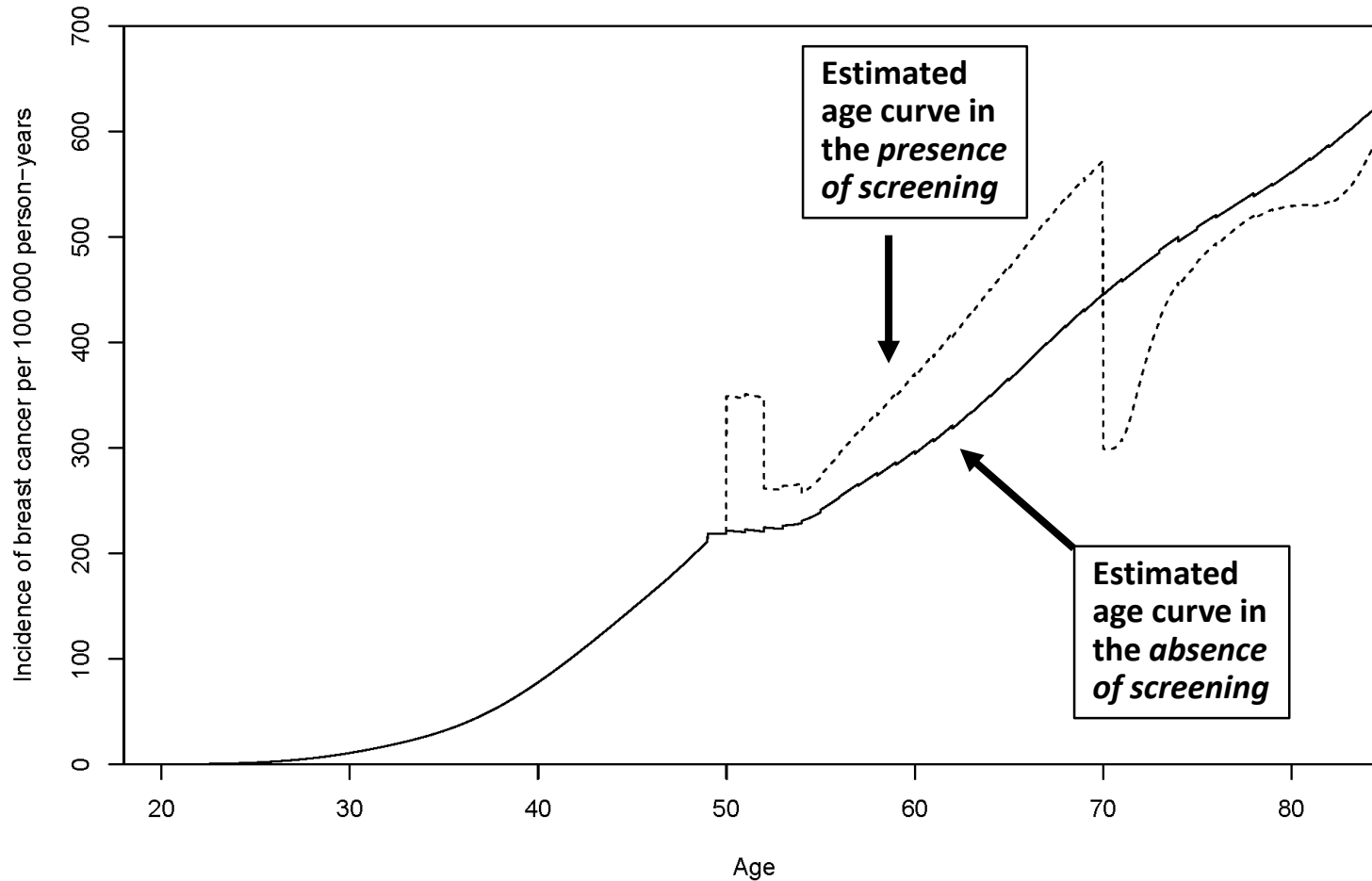
(PMID: 37403150)

$$R_{c,p,r} = \exp(A_a + ns(A_a, kn_a) + ns(P_p, kn_p) + ns(C_c, kn_c) + S_1 * scr_1 + S_2 * scr_2 + S_{3+} * scr_{3+} + (A_a * scr_{3+}) + (S_{post} * scr_{post} + ns(timeScr_{post}, kn_{scr_{post}}) * scr_{post}) + H * ht + County_r)$$

where  $R_{c,p,r}$  is the breast cancer incidence rate in birth cohort  $c$  at period  $p$  for county(region)  $r$ ,  $A_a$  is the age component for age  $a = p - c$ ,  $P_p$  is the period component for period  $p$ , and  $C_c$  is the cohort component for birth cohort  $c$ , and  $ns(\dots)$  denotes a natural cubic splines function. For the age component we specified inner spline knots at age 50, 52, 54, 56, 60, 70 and 80 years ( $kn_a$ ). We used three degrees of freedom for the period and birth cohort components, both with knots set at the corresponding quantiles (defined as  $kn_p$  and  $kn_c$ , respectively).  $S_1$ ,  $S_2$ ,  $S_{3+}$  and  $S_{post}$  are coefficients for the corresponding  $scr_1$ ,  $scr_2$ ,  $scr_{3+}$  and  $scr_{post}$ , screening variables.  $scr_1$  reflects initial screening,  $scr_2$  first subsequent screening,  $scr_{3+}$  continued screening, and  $scr_{post}$  previous screening. For previous screening  $timeScr_{post}$  is the time since screening ceased, and we specified inner spline knots at 2, 5, 10 and 13 years ( $kn_{scr_{post}}$ ) for  $timeScr_{post}$ . In addition,  $H$  is the coefficient for the hormone therapy variable  $ht$ . Each county got its own level as given by the  $County$  variable, while the logarithm of the number of person-years under study was used as offset adjusting for variations in person-years.

# Results:

- Estimated age curve with and without screening

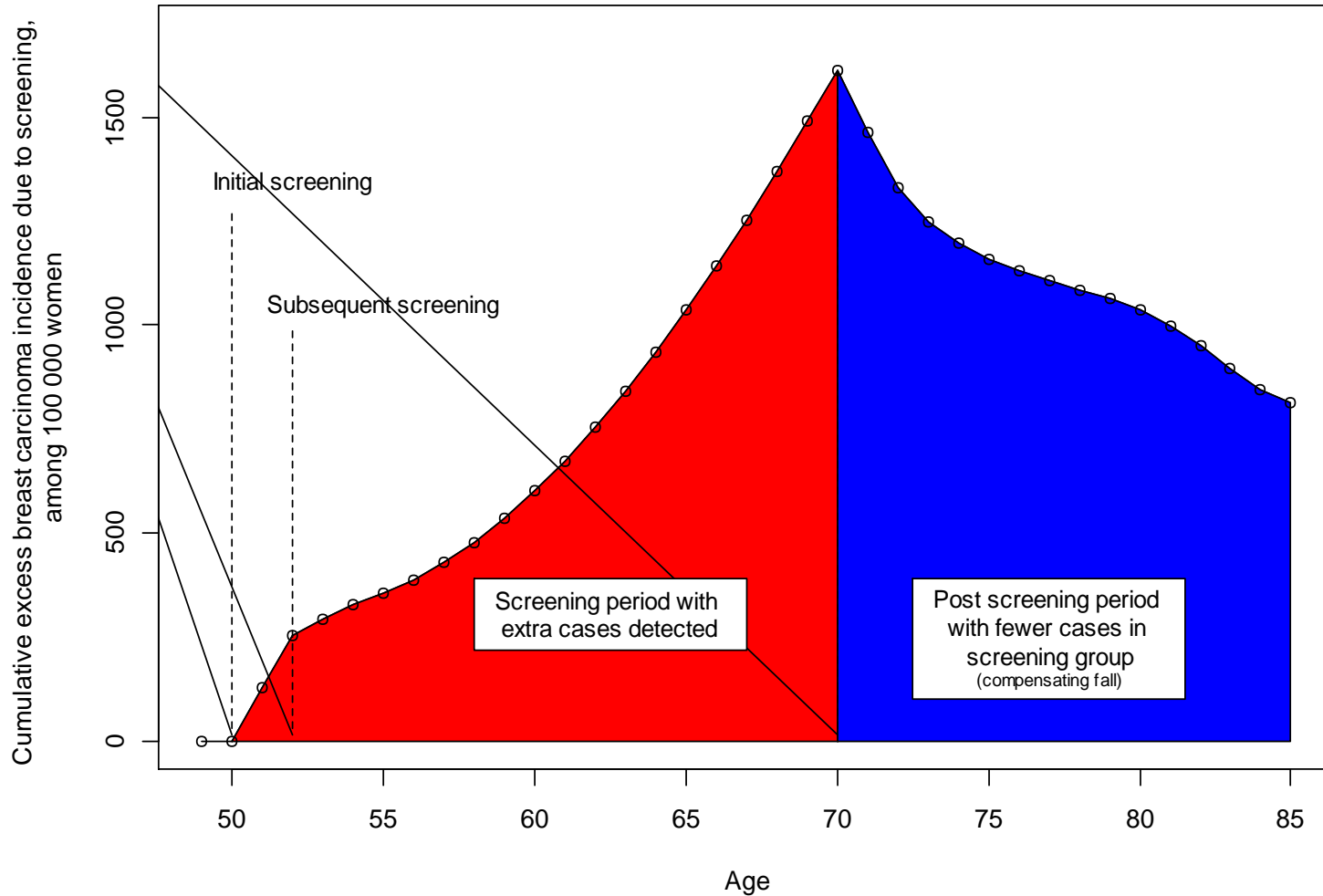


# Results

We estimated that:

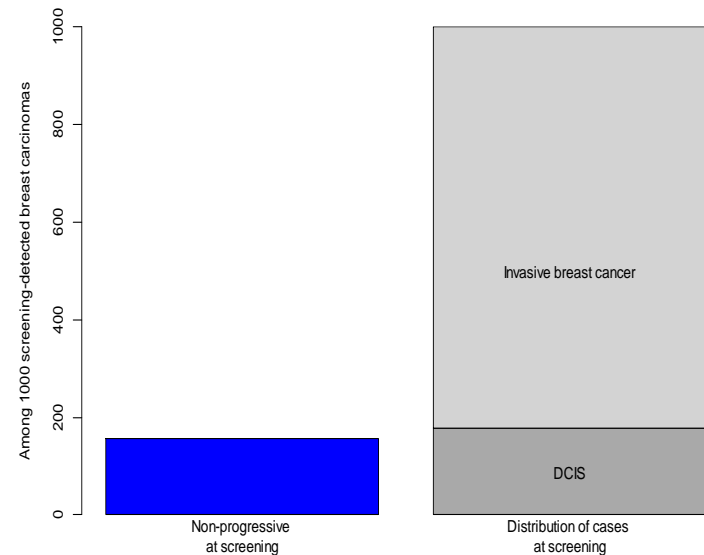
- **15.7% [95% CI 3.3-27.1] of carcinomas detected at screening** is estimated to be non-progressive by age 85
- **1.1% of screening participants is diagnosed with a breast carcinoma that is non-progressive by age 85.**
- About 50% of the excess incidence detected during screening did not progress to clinical cancer by age 85.

# What's behind the estimate?



# Is the non progressive cancers DCIS?

**It may all be DCIS,**  
but its not possible  
to separate out DCIS  
using population data



# Conclusions

- **Nearly one in six breast carcinomas detected at screening may be non-progressive** (by 85 years of age)
- Our estimates of non-progression are lower than some previous studies
- We need better clinical understanding of tumor progression.  
(but how?)

# Next

- **Overdiagnosis** is not only non-progressive cancers
- Women can die of other causes before the breast carcinoma gives clinical symptoms

... new publication soon to be submitted to journal!

(full manuscript is ready for submission)

# The scientific paper:

"Non-progressive Breast Carcinomas Detected at Mammography Screening: A Population Study",  
Heggland, T. et al, Breast Cancer Research, 2023.  
<https://pubmed.ncbi.nlm.nih.gov/37403150/>



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# Questions?



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