



**New Cancer Screening Programmes  
Stockholm, 6 October 2016**

**How to plan for evaluation of a  
new screening programmes**

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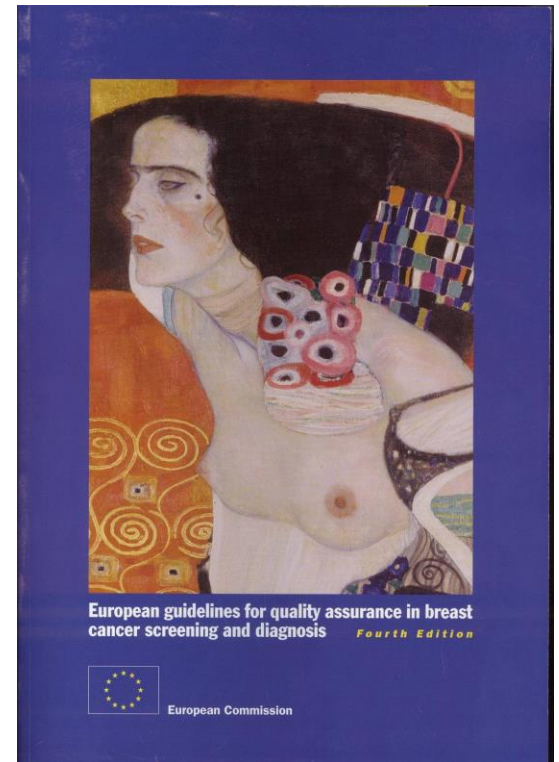
# Conflicts of interest

- Meeting participation with Roche and Astra-Zeneca with fees paid to the University of Copenhagen
- Collaborate with Biomediq, no fees and/or stocks

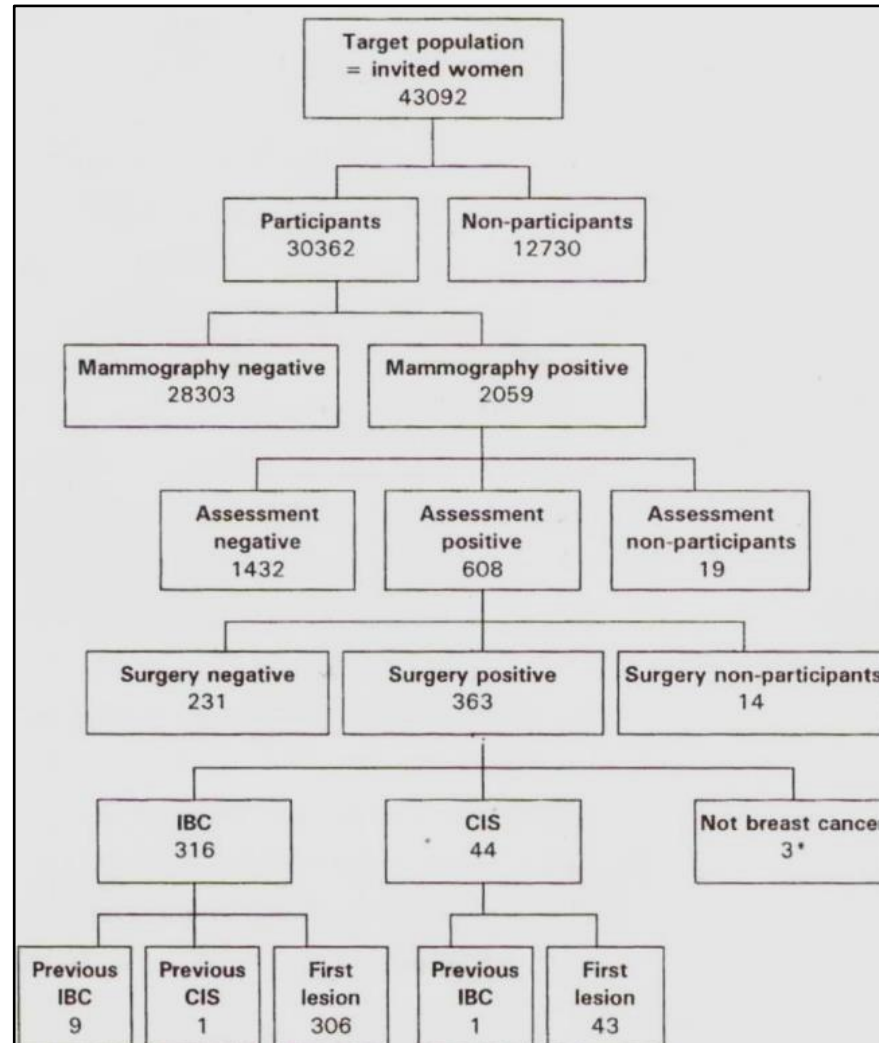
# Evaluation

E. g. Breast screening - What do we want to know?

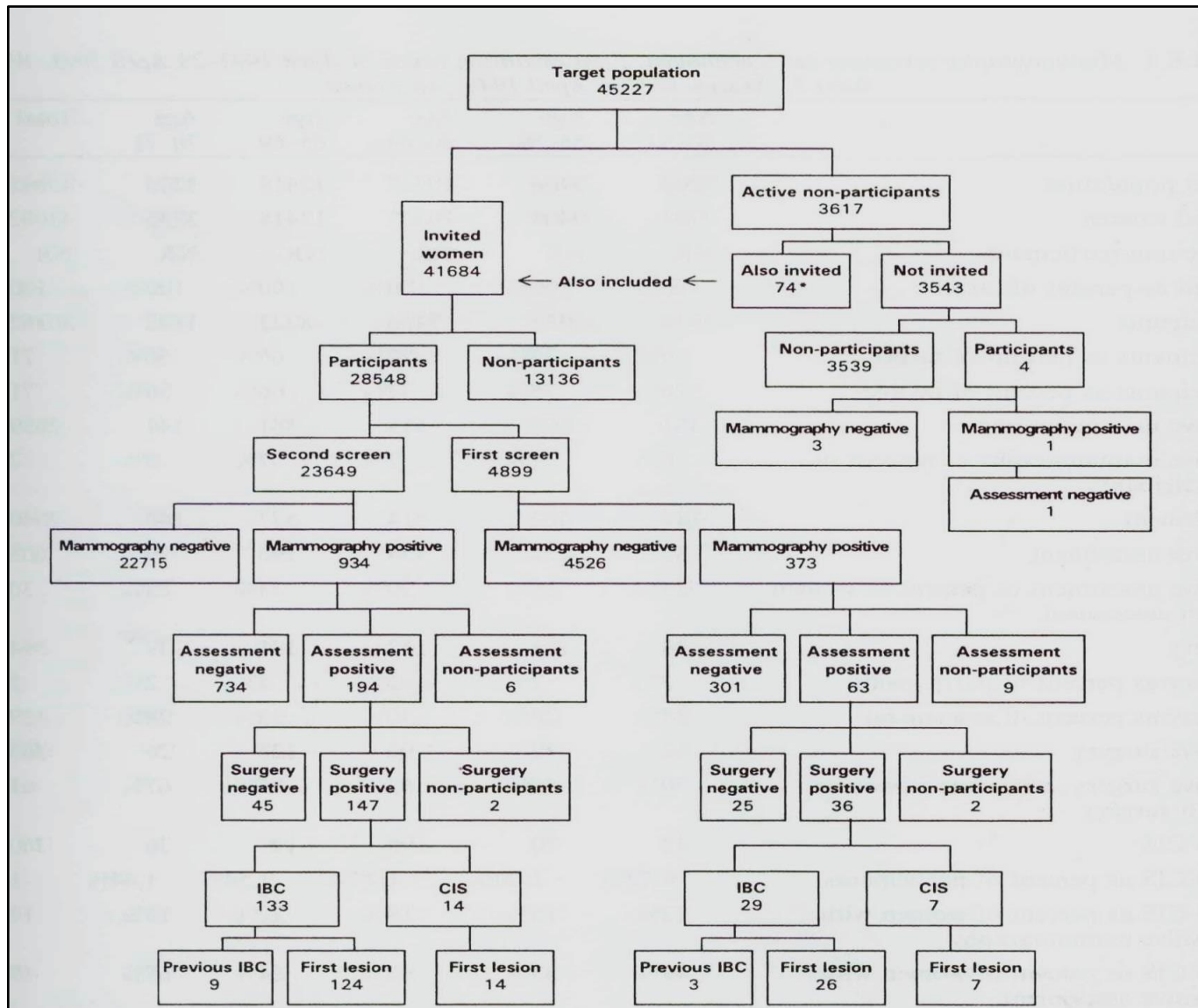
- **Short-term** quality assurance indicators
- E. g. European Guidelines
- Proportion of women invited that attend for screening
- Proportion of women recalled for further assessment
  - initial screen
  - subsequent screen
- Breast cancer detection rate
- **Long-term** outcome
- Did the screening program result a reduction in the disease-specific mortality?



# First invitation round



# Second invitation round



# Breast screening database

## PERS

Municipality code  
Institute code  
Personal identification  
Creation date  
Invitation round  
Invitation date  
Region on CPH  
Referral to Rigshospitalet  
Vital status  
Date of vital status  
DBCg type  
DBCg date  
....

## HISPERS

Municipality code  
Institute code  
Personal identification  
Invitation date  
Invitation round  
Creation date  
Region in CPH  
Referral to Rigshospitalet  
Vital status  
Date of vital status  
DBCg type  
DBCg date  
Invitation not wanted  
Date of this

## MAMMO

Municipality code  
Institute code  
Room number  
Screening date  
Time for end  
Day of week  
Personal identification  
Invitation round  
Screening type ½  
Result  
Assessment  
Surgery  
Date for assess  
Date for surgery  
Date answer mammo  
Mail/telephone

# E. g. Detection rate

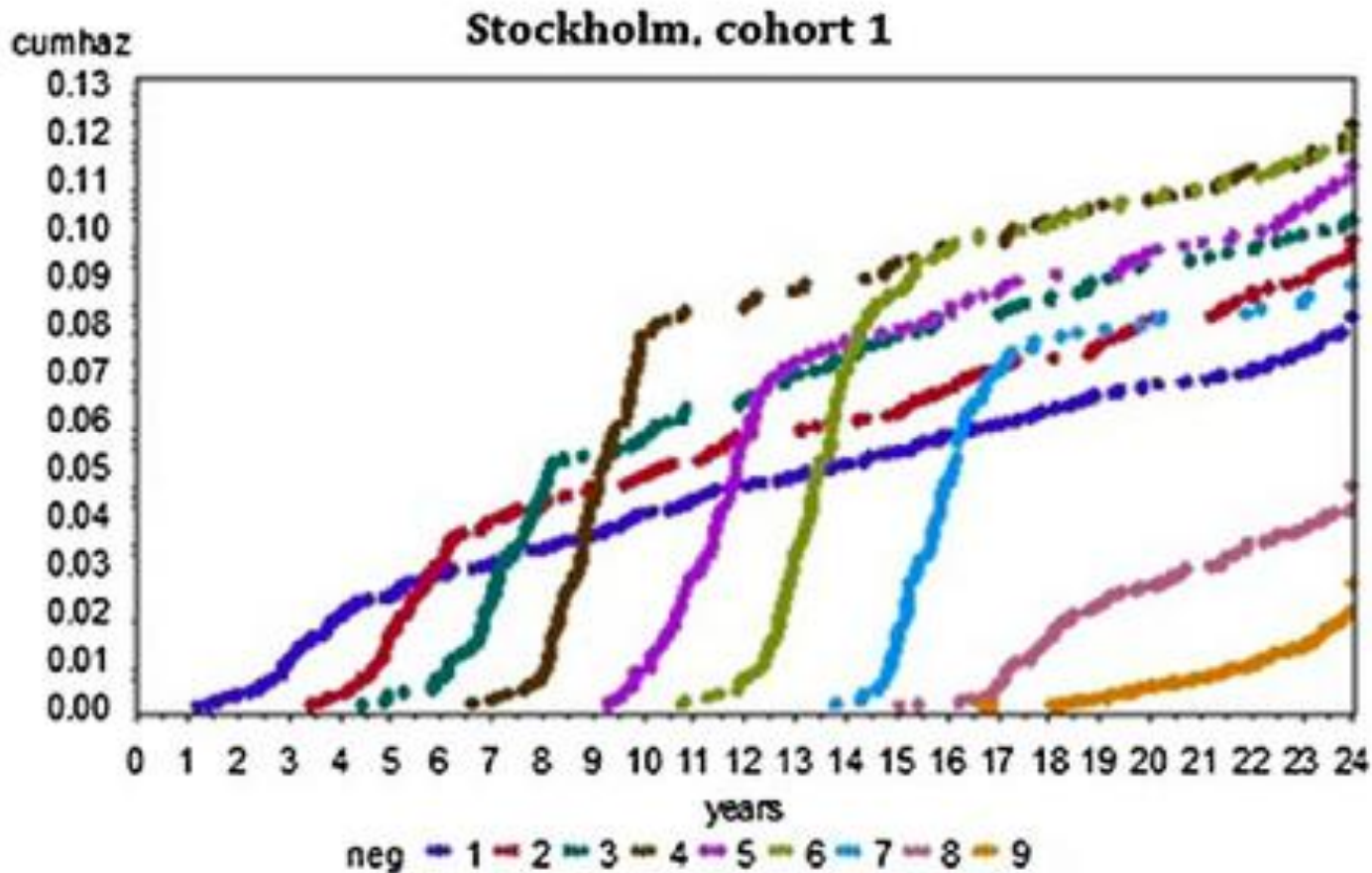
Detection rate invasive + CIS, first four invitation rounds, Copenhagen, Denmark

Invitation round	Screen number				1-4
	1	2	3	4	
1	11.9				11.9
2	6.7	6.1			6.3
3	6.3	6.5	6.0		6.1
4	4.5	3.1	5.4	6.4	5.4
1-4	10.0	5.8	5.9	6.4	7.6

Vejborg et al, 2002

# E. g. Cumulative hazard

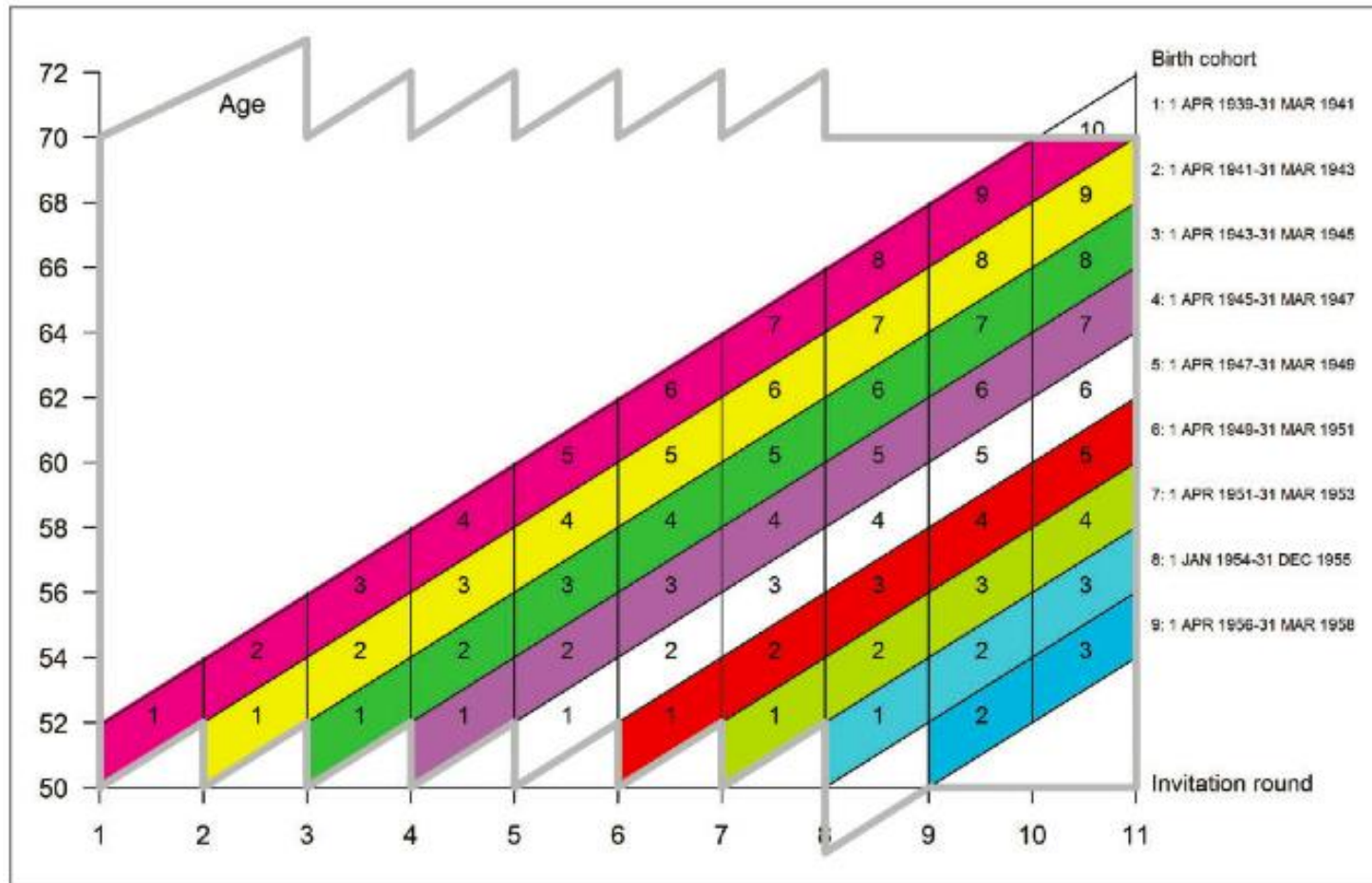
by number of previous negative screens



Andersen et al, 2015



# E. g. Coverage by invitation and participation rate, Copenhagen, Denmark



### Coverage by invitation

Cohort number	Invitation round						
	1	2	3	4	5	6	7
1	96	94	90	88	87	70	68
2	100	92	89	89	69	68	
3	96	94	92	72	70		
4	96	93	78	76			

### Participation rate

Cohort number	Invitation number						
	1	2	3	4	5	6	7
1	76	70	73	72	71	85	83
2	71	70	70	68	83	84	
3	69	68	78	78	82		
4	67	66	70	75			

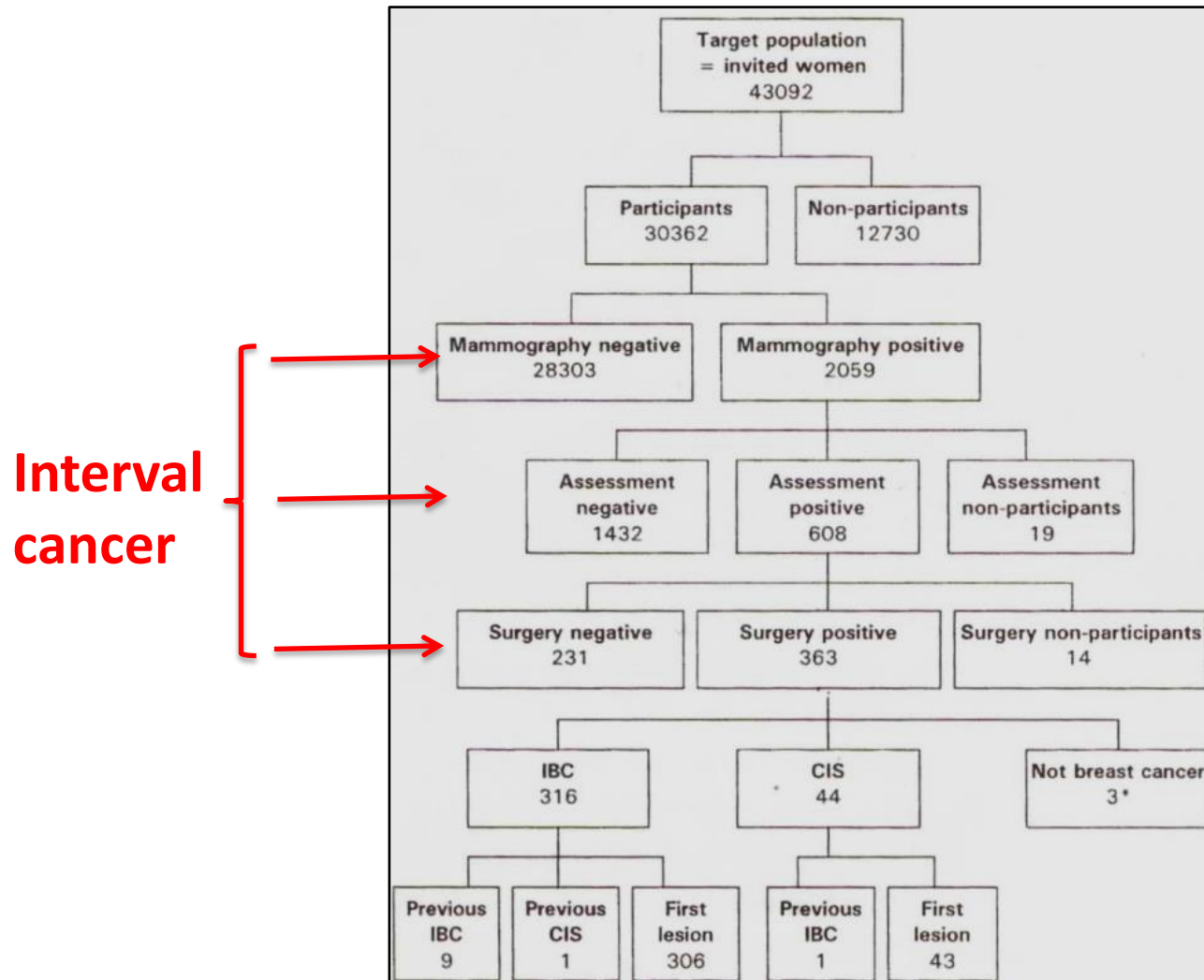
# Extract from existing databases

- CPR, central population register
- Booking system
- RIS, x-ray examination register
- NPR, national patient register
- Patobank
- CPR → booking system → invitation
- RIS → NPR → screening mammography
- Definition participation:
- Date of (DZ123AA, DZ123A, DZ108A, UXRC45)  $\geq$  Date of invitation and before next invitation/2 years



# Interval cancer

Definition from screening database



# Interval cancer

## Present definition

- NPR code ZPR01N (normal) and Patobank SNOMED code (T04''' & (M8'''3, M8'''6, M9'''3)) before next booking date/screen date/2 years
- Or
- NPR code ZPR00N (abnormal) and Patobank SNOMED code (T04''' & (M8'''3, M8'''6, M9'''3)) >6 months after screen date and before next screen/2 years
- This means that screen-detected breast cancers with assessment/surgery >6 months will be defined as interval cancers, and non-screen-detected breast cancers rising <6 months after last screen will be defined as screen-detected

# Danish Breast Screening Program

## Reported indicators

	Standard	Round 3 2012-14	Round 2 2010-11	Round 1 2008-09
Radiation dose	<2.0 mGy	NR	NR	NR
Participation/invited	>75%	84	82	77
Participation/targeted	none	75	72	75
Screening interval 2 years	>98%	74	52	NR
Recall	<3%	2.7	2.7	3.0
Interval cancer 0-11 md	<30%	26	26	27
Interval cancer 12-23 m	<50%	50	37	41
Invasive/(Invasive + DCIS)	>80%/<90%	86	86	86
Node negative	>75%	82	79	68
Small, max 10 mm	>30%	40	40	37
Benign vs malign surgery	Max 1:4	1:8.1	1:6.9	1:1.6

# Danish Breast Screening Program

Examples of technical problems in reported indicators

- “It has turned out that Region South from mid round 3 for technical reasons registered a screen with the code DZ123 instead of DZ123AA...”
- Benign-to-malignant-ratio round 2 reported to 1:8.3 in 2013 and to 1:6.9 in 2015. “Changed data definition. Previous: NPR used. Now: a tumor reported as benign in NPR but malignant in Patobank, defined as malignant.”
- Node negative tumors reported to 70% in 2013 and to 79% in 2015. Definition changed, e.g. lymph node info from Patobank included even if no operation code in NPR

# Long-term outcome

## Data required

### Breast cancer mortality:

- Identify target population
- Follow-up for death and immigration
- Causes of death
- Breast cancer incidence (to calculate incidence-based-mortality)

### Overdiagnosis:

- Follow-up for death and immigration
- Breast cancer incidence (to calculate cumulative breast cancer incidence)

### Expected outcome in absence of screening:

- Before, non-screening region, non-participants

### Methodology:

- Routine or incidence-based-mortality; fixed age-groups or cohorts



# Long-term outcome

Denmark had 17 years between first and last screened regions

	Before screening	During screening
Screening region (Copenhagen and Fyn)	Historical Control group	Study group
Non-screening region (Rest of Denmark)	Historical, regional control group	Regional Control group

RRR: ((Study group/Historical control group)/  
(Regional control group/Historical regional control group))

# Long-term outcome

## Individual cohort data

	Copenhagen	Fyn
Reduction in breast cancer mortality		
- Invited women	25%	22%
- Screened women	37%	28%
Increase in breast cancer incidence*		
- Invited women	3.4%	0.7%
- Screened women	5%	1%

\* With at least 8 years post-screening follow-up

Olsen et al, 2005; Njor et al, 2013; Njor et al, 2015

# Long-term outcome

## Routine data

- “We were unable to detect any effect of the Danish screening programmes on breast cancer mortality” (Jørgensen et al, 2010)
- Based on routine data including deaths in women diagnosed before screening start
- Focused on similarity of annual changes (= slopes) in trends of death rates in screening and non-screening regions from pre-and post-screening periods
- Ignored a statistically significant change in relative level of breast cancer mortality occurring between the pre-and post-screening periods
- “One in four breast cancers diagnosed in the screening age in the Danish screening programme is overdiagnosed” (Jørgensen et al, 2009)
- About half of observations in age-group 70-79 contributed limited to compensatory dip
- Pre-screening differences between regions were not taken into account

# Conclusion

- Use of data from existing registers for evaluation avoids double registrations and ensures consistency between evaluations
- But may lead to technical problems with definitions and transfer between data bases
- A dedicated screening database might be the optimal starting point unless people with very good inside into all databases undertake the evaluation
- Analysis of data by different groups of researchers can serve as mutual check for interpretation of data

**Thank you for your attention**



**Copenhagen Old Municipality Hospital, now part of University of Copenhagen**