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Breast Cancer Screening: Dutch Experience

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Breast Cancer Screening

Target population: women aged 50-75

Invitation every two years

1.2 million of women are invited every year

Invitation by letter, with explanation in 5 languages

3 weeks before the appointment

One reminder

About 950.000 are participating (80%)

Costs are covered by the government

Breast Cancer Screening

The programmatic Dutch Breast Screening Program started in 1990

Based on criteria formulated by Wilson and Jungner

1. Relevance: disease is an important health problem
2. Treatable: disease must be treatable with a generally accepted treatment
3. Health infrastructure: there should be sufficient infrastructure for diagnosis
4. Recognizable: there should be a recognizable latent stadium of the disease
5. Natural course: the natural course of the disease should be known
6. Illness: there should be consensus as to who is ill or most at risk
7. Screening test: the screening test should be easy to use
8. Acceptability: the screening test should be acceptable for the general population
9. Cost-benefit: cost should be at least equal to the benefits
10. Continuity: the screening process must be continuous.

Breast Cancer Screening

Goal of the screening program: to detect breast cancer in an early stage.

Early detection leads to a better prognosis, less invasive treatment options and decreased breast cancer mortality.

On behalf of the Dutch Ministry of Health the Program is financed and coordinated by the Centre for Population Screening of RIVM.

The Dutch Screening Programs are secured by 4 important public values:

1. Effectiveness
2. Quality: safe, national protocol, uniform, and good alliance with health care
3. Affordability: efficiency and cost-effectiveness
4. Accessibility: close to participant, free of cost, free choice, timely

Organization of Breast Cancer Screening

The Health Council

provides scientific advice for the Minister of Health

Minister of Health

decides on introduction of and/or innovations in screening programs.

The Centre for Population Screening of RIVM

finances, coordinates and directs the program, stakeholders and partners.

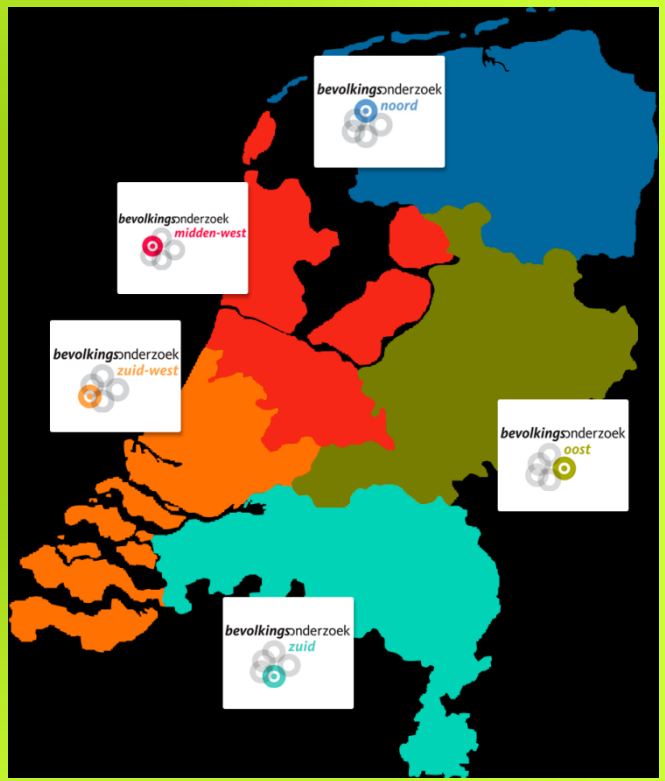
is responsible for setting quality standards, organizing monitoring and evaluation, organizing uniform information for the public and for involved professionals, coordination of knowledge (practical en scientific), and development and improvement of the programs.

The Health Inspection is overlooking the whole chain of integrated care.

Organization of Breast Cancer Screening

The regional screening organizations are responsible for the practical execution of the program and are:

- owner of the mobile units
- owner of the mammographs
- hiring screeners
- contracting radiologists
- in charge of IT system
- in contact with clients
- in contact with municipalities
- in contact with regional hospitals and GP's



Organization of Breast Cancer Screening

Key elements of the program are:

the independent positions of

- the National Expert and Training Centre for Breast Cancer Screening (LRCB)
  - to optimize and secure the quality of the program
- the National Evaluation Team for Breast Cancer Screening in the Netherlands (NETB)
  - to monitor and evaluate the effectiveness of the program

Breast Cancer Screening

Two view digital mammography

Organization of Breast Cancer Screening

Two radiologists independently review the screens.

To improve sensitivity: If there are previous screens, there is a comparison with those.

If there is any abnormality the radiologists discuss their findings.

If there is no abnormality: the women will receive a letter within 10 days

If there is an abnormality: the GP will contact the women within 10 days

Organization of Breast Cancer Screening

In case of an abnormal finding: the women will be referred to the hospital

There she will receive investigations:

- Physical examination
- Mammagraphy
- Ultrasound, MRI, Biopsy ….

This is NOT part of the population screening on breast cancer. So, the costs should be covered by the own insurance.

Breast Cancer Screening: FACTS

- Target population: women aged 50-75 years
- Invitation every 2 years: 1.1 million women
- 80% attendance rate (participation n=950.000)
- Screen detected cancers in target population: 5500
- Referral rate per 1000 women screened: 20,2
- Program sensitivity: 71,5% (2/3 detected)
- Regular participation leads to 50% risk reduction in mortality
- Lives saved per year: n=775
- Overdiagnosed: n=375
- Cost: €60 million per year
- € 55-60 per examination

Breast Cancer Screening: FACTS

Table 1. Program sensitivity and specificity

Per 1000 women

		Truth	
		+	-
Test	+	True pos: 6	False pos: 14
	-	False neg: 2	True neg: 978

Sensitivity: 6/8=75%

Specificity: 978/992=98.6%

Breast Cancer Screening: Advantages

- Health gain
- Risk reduction
- Less invasive treatment
- More treatment options
- Reassurance

Breast Cancer Screening: Disadvantages

- False-positive results
- False-negative results
- Overdiagnosis and overtreatment
- No guarantees
- Radiation / tests in healthy people
- Mammography is a painful method

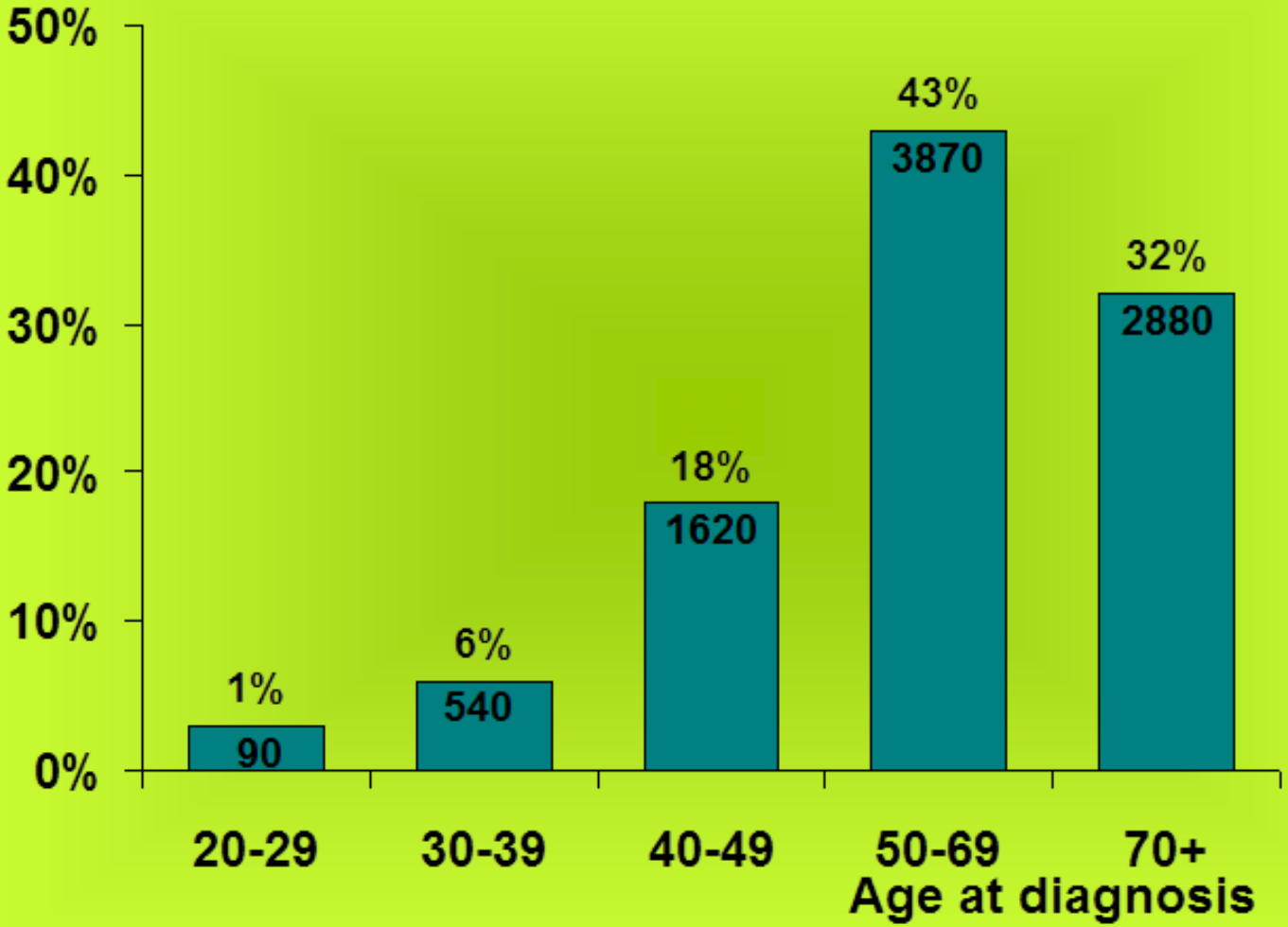
Factors for success in the Netherlands

- Favorable geography NL
- National management by Centre for Population Screening
- National independent reference center
- National independent evaluator
- Invitation according to postal regional code
- Mobile units in communities
- Organized separate from health care (women are not (yet) patients but clients)
- Recently: digitalization
- National advisory committees, consisting of the involved public and private organizations, advise the Centre for Population Screening on a regular basis

Factors for success in the Netherlands

Mobile breast screening unit is located in neighbourhoud

Lowering the starting age?



Lowering the starting age?

A modeling study to evaluate the costs and effects of expanding the lower age limit of population breast cancer screening

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Lowering the starting age? - Methods

Markov Simulation Model on Radiation Risk in breast cancer Screening (SiMRiSC) with 3 model components

Carcinogenesis

- Risk to develop breast cancer during life (mutation, age)
- Preclinical tumor growth
- Tumor induction (dose)

Detection

- Sensitivity & specificity of mammography and breast density
- Costs of screening, diagnostics, treatment and hospital stay (tumor size)

Death

- Breast cancer death (lymph nodal status, tumor size, age)
- population death rate (age)

Lowering the starting age? - Methods

Objective: To evaluate the benefits, harms, and cost-effectiveness of lowering the starting age of breast cancer screening in the Dutch general population

Economic modeling analysis with a lifelong perspective

Scenarios in the model:

- Biennial screening from 48-74
- Biennial screening from 46-74
- Reference: the current Dutch breast cancer screening program

Lowering the starting age? - Methods

A validated version of a simulation model (SiMRiSc) was applied to evaluate screening scenarios with lower starting ages

Data sources from published data

Main outcome measure

- Estimated health benefits:
  - tumor deaths prevented, years of life saved (YOLS)
- Harms:
  - false positives, radiation-induced tumors; costs combined to incremental costs-effectiveness ratios (ICERs)

Lowering the starting age? – Procedure

Women are simulated during their lifetime taking into account

- their life expectancy
- chance of developing a tumor, including risk of tumor induction due to diagnostic radiation
- tumor growth
- survival from breast cancer

In the simulation every woman is given a predetermined natural death age which is sampled from the life expectancy in the Netherlands.

Lowering the starting age? – Procedure

The breast cancer incidence rate is sampled to assign to women an individual probability to develop breast cancer at a given age.

For each women it is determined at which age the tumor would be clinically detected.

This is dependent on

- tumor growth model
- and the tumor size at clinical (self) detection

Lowering the starting age? – Procedure

The tumor growth has an age dependent volume doubling time and is sampled from a log-normal distribution.

The preclinical period of the tumor is defined as the time from which the tumor size is larger than the minimal detection threshold for mammography (5mm) until the time of clinical detection without screening is also sampled from a distribution.

Lowering the starting age? – Procedure

If a tumor is present at the screening moment, the chance of detection is dependent on the mammographic sensitivity.
This is determined by age and breast density.

If a tumor is found, either by screening or self-detection, the woman will be removed from the simulation and the breast cancer specific death age of the woman will be calculated based on the life expectancy after breast cancer diagnosis depending on the tumor size at clinical detection.

Lowering the starting age? – Model input

Parameters		Value (95% CI)		
Tumor induction model	Dose [mSv]	3 (1-5)		
	Probability of tumor induction [%]	0.51 (0.28-0.83)		
Tumor growth model	Tumor doubling time	days	Mean, log transformed	Spread
	<50 years	80	4.38 (3.78-4.99)	0.43
	50-70 years	157	5.06 (4.80-5.32)	0.17
	>70 years	188	5.24 (4.79-5.69)	0.23

Lowering the starting age? – Model input

Self-detection model	**Self-detection diameter [cm]**	μ	2.87 (2.86-2.88)
		σ	0.61 (0.51-0.70)
Cumulative incidence rate	f [%]	22.6 (21.1-24.0)	
	m [years]	72.9 (70.7-75.1)	
	s [years]	21.1 (19.3-22.9)	

Lowering the starting age? – Model input

	BI-RADS density score	1	2	3	4
Distribution of breast densities	<40 years [%]	4.4	30.2	48.2	17.2
	40-50 years [%]	5.9	34.1	46.9	13.1
	50-60 years [%]	8.5	50.3	36.6	4.6
	60-70 years [%]	14.9	53.4	29.4	2.3
	>70 years [%]	17.4	54.3	26.2	2.1

Lowering the starting age? – Model input

BI-RADS density score	1	2	3	4
Sensitivity [%]	87 (75.2-98.8)	84 (80.1-87.9)	73 (54.8-91.2)	65 (34.0-96.0)
Specificity [%]	96.5 (96.0 – 96.9)			

Lowering the starting age? – Validation

The model was validated by comparing the estimates of the simulated outcomes in the reference scenario the observed data from the Dutch national screening program.

This was done for

- number of screen detected tumors
- tumor size distribution
- number of interval cancers
- number of false positive tests

Lowering the starting age? – Validation

	simulated	observed
Number of screen detected tumors (first round)		
50-54	234	263 (231-295)
55-59	12	19 (10-28)
60-64	7	19 (11-27)
65-69	4	6 (1-11)
70-74	2	5 (1-9)

Lowering the starting age? – Validation

	simulated	observed
Number of screen detected tumors (further rounds)		
50-54	588	531 (486-576)
55-59	816	760 (706-814)
60-64	964	1029 (966-1092)
65-69	864	852 (795-909)
70-74	662	703 (651-755)

Lowering the starting age? – Costs

Procedure	Costs (in Euro/2013)
Screening and diagnosis	
Mammogram	64
Biopsy	176
Treatment by tumour size	
Treatment <2cm	6438
Treatment 2-5cm	7128
Treatment >5cm	7701

Lowering the starting age? – Results

	Scenario (start age-end age)	
	46-74 vs 48-74	48-74 vs 50-74
Outcomes		
Screen detected tumours (N)	+ 3.5% (593)	+ 4.0% (573)
Tumor size distribution		
<2 cm	+ 3.3% (571)	+ 4.3% (553)
2 – 5 cm	- 10.0% (22)	- 4.8% (20)
≥5 cm	- 32.6% (0.57)	- 40.3% (0.43)
Interval cancers (N)	+ 8.7% (288)	+ 9.5% (265)
Expected benefits		
Tumor deaths prevented (N)	+ 5.1% (104)	+ 6.5% (99)
YOLS	+ 7.2% (1478)	+ 10.9% (1379)
YOLS (discounted)	+ 23.9% (635.9)	+ 13.4% (582.1)

Per 10.000 simulated women

Lowering the starting age? – Results

	Scenario (start age-end age)	
	46-74 vs 48-74	**48-74 vs 50-74**
Expected harms		
False positives (N)	+ 8.8% (4089)	+ 9.2% (3760)
Radiation-induced tumors (N)	+ 12.5% (36)	+ 14.3% (32)
Costs and cost-effectiveness		
Total costs/ million €	+ 4.0% (17.2)	+ 4.1% (16.5)
Total costs (discounted)/ million €	+ 11.4% (12.5)	+ 5.5% (11.8)
Incremental C.E. Ratio	6.8	5.1
Incr. C.E. Ratio (discounted)	12.9	9.4

Per 10.000 simulated women

Lowering the starting age? – Conclusion

Women could benefit from lowering starting age of screening

- more small tumours will be detected
- more breast cancer deaths will be averted
- at reasonable additional costs

Biennial screening 48-74 is more cost-effective than biennial screening 46-74
However the 46-74 scenario is still cost-effective and adds on averted tumour deaths.

Lowering the starting age? – Conclusion

In both alternative scenarios

- the number of additional expected harms is relatively small
- difference in ICERs is not large

Introducing two additional screening rounds to the current biennial breast cancer screening in the Netherlands is justifiable from a cost-effectiveness and benefit-harms point of view

::The END::

Thank you for your Attention!

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