

2930 women with breast cancer diagnosed in
Finland in 1991 or 1992

Excluded

Clinical data not available,
n=274

Included

Inclusion criteria fulfilled,
current place of
residence within the
specified regions, n=186

Excluded

Excluded

Method of detection not
known, n=49

Excluded

One or more classification
marker not available,
n=747

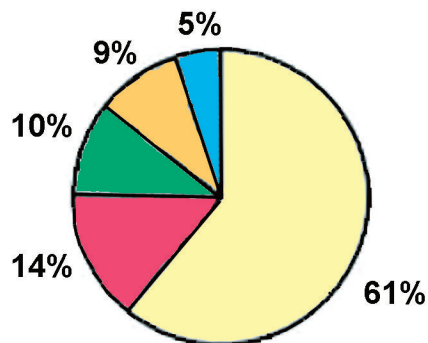
DCIS, n=203
Distant metastases at
diagnosis present, n=136
Bilateral breast cancer,
n=261
Other malignancy, n=235
No breast surgery, n=42

Found in mammography
screening, n=247

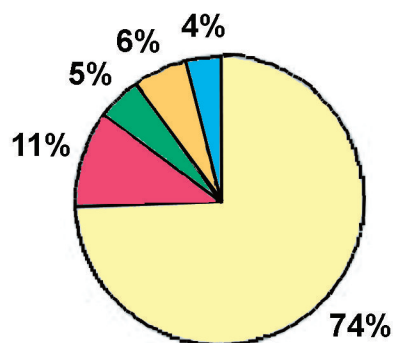
Found outside of
screening, n=989

A

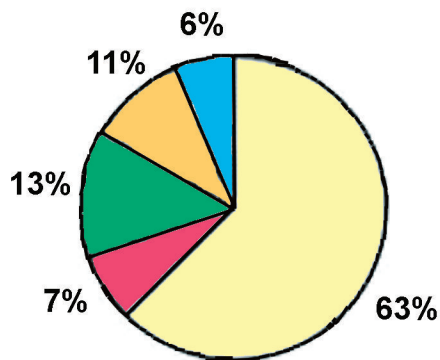
Age ≤ 49 years,
found outside of screening

**B**

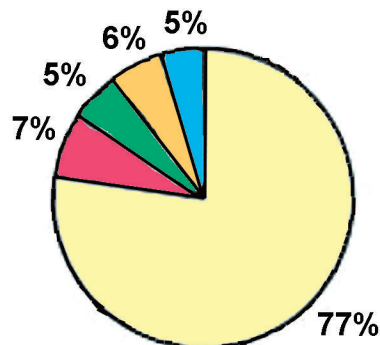
Age 50 to 69 years,
found in screening

**C**

Age 50 to 69 years,
found outside of screening

**D**

Age ≥ 70 years,
found outside of screening



Supplementary Figure Legend

Supplementary Figure 1. The CONSORT diagram of the study.

Supplementary Figure 2. Breast cancer molecular subtypes by age at diagnosis and the method of cancer detection; classification based on immunohistochemical assessment of HER2 expression. Panel A: age ≤ 49 years, found outside of screening; B: age 50 to 69 years, found in screening; C: age 50 to 69 years, found outside of screening; and D: age ≥ 70 years, found outside of screening.

Supplementary Table 1. Expression of 12 proteins and presence of *HER2* amplification

Marker		Breast cancer molecular type*					<i>P</i>	
		Luminal A	Luminal B	HER2+/ER-	Basal-like	Nonexpressor		
		No. (%) n = 844	No. (%) n = 118	No. (%) n = 120	No. (%) n = 98	No. (%) n = 56		
<i>Classifier markers</i>								
ER	negative	55 (7)	12 (10)	120 (100)	98 (100)	56 (100)		
	positive	765 (93)	105 (90)	0 (0)	0 (0)	0 (0)		
	NA**	24	1	0	0	0		
PR	negative	189 (23)	48 (42)	120 (100)	98 (100)	56 (100)		
	positive	620 (77)	67 (58)	0 (0)	0 (0)	0 (0)		
	NA	35	3	0	0	0		
HER1	negative	559 (92)	91 (91)	69 (67)	13 (14)	56 (100)		
	positive	46 (8)	9 (9)	34 (33)	79 (86)	0 (0)		
	NA	239	16	17	6	0		
<i>HER2</i> ampli- fication	negative	844 (100)	0 (0)	0 (0)	98 (100)	56 (100)		
	positive	0 (0)	118 (100)	120 (100)	0 (0)	0 (0)		
	NA	0	0	0	0	0		
CK5/6	negative	658 (99)	100 (99)	98 (93)	37 (44)	56 (100)		
	positive	9 (1)	1 (1)	7 (7)	48 (54)	0 (0)		
	NA	177	17	15	13	0		
<i>Other markers</i>								
HER2 (IHC)	negative	766 (96)	36 (31)	16 (13)	90 (93)	53 (96)	<0.0001	
	positive	35 (4)	81 (69)	103 (87)	7 (7)	2 (4)		
	NA	42	1	1	1	1		
Ki-67	low	578 (78)	53 (47)	37 (32)	23 (25)	27 (50)	<0.0001	
	high	165 (22)	59 (53)	78 (68)	69 (75)	27 (50)		
	NA	101	6	5	6	2		
TP53	negative	671 (92)	76 (69)	59 (56)	45 (48)	37 (76)	<0.0001	
	positive	58 (8)	34 (31)	47 (44)	49 (52)	12 (24)		
	NA	115	8	14	4	7		
GATA3	negative	72 (10)	11 (11)	53 (50)	78 (90)	23 (41)	<0.0001	
	positive	652 (90)	90 (89)	52 (50)	9 (10)	30 (54)		
	NA	120	17	15	11	3		
CK18	negative	6 (1)	1 (1)	2 (2)	22 (24)	8 (15)	<0.0001	
	positive	752 (99)	105 (99)	103 (98)	68 (76)	47 (85)		
	NA	86	12	15	8	3		
KIT	negative	639 (95)	97 (95)	95 (90)	65 (70)	48 (91)	<0.0001	
	positive	36 (5)	5 (5)	11 (10)	28 (30)	5 (9)		
	NA	169	16	14	5	3		
SMA	negative	734 (91)	108 (98)	104 (96)	73 (89)	50 (91)	<0.0001	
	positive	9 (1)	2 (2)	4 (4)	9 (11)	5 (9)		
	NA	101	8	12	16	1		
COX2	negative	562 (67)	59 (50)	50 (42)	35 (36)	25 (46)	<0.0001	
	positive	275 (33)	58 (50)	68 (58)	62 (64)	29 (54)		
	NA	5	1	2	1	2		

*Luminal A: ER+ and/or PR+, HER2-; luminal B: ER+ and/or PR+, HER2+;
HER2+/ER-: HER2+, ER-, PR-; basal-like: ER-, PR-, HER2-, cytokeratin 5/6 and/or HER1+;
unclassified: ER-, PR-, HER2-, HER1- and cytokeratin 5/6-
**NA, not available

Supplementary Table 2. Distribution of breast cancer molecular subtypes by age at detection and the method of detection.

Molecular type	Age ≤ 49 , found outside of screening N=320* n (%)	Age 50-69, found outside of screening N=348 n (%)	Age 50-69, found in screening N=206 n (%)	Age ≥ 70 , found outside of screening N=321† n (%)
Luminal A	198 (61.8)	222 (63.8)	151 (73.3)	242 (75.4)
Luminal B	41 (12.8)	24 (6.9)	22 (10.7)	29 (9.0)
<i>HER2+</i> /ER-	39 (12.2)	48 (13.4)	11 (5.3)	19 (5.9)
Basal-like	28 (8.8)	35 (10.1)	15 (7.3)	18 (5.6)
Nonexpressor	14 (4.4)	19 (5.5)	7 (3.4)	13 (4.0)

*32 cases were found in mammography screening in age group ≤ 49 (not shown)

†9 cases were found in mammography screening in age group ≥ 70 (not shown)