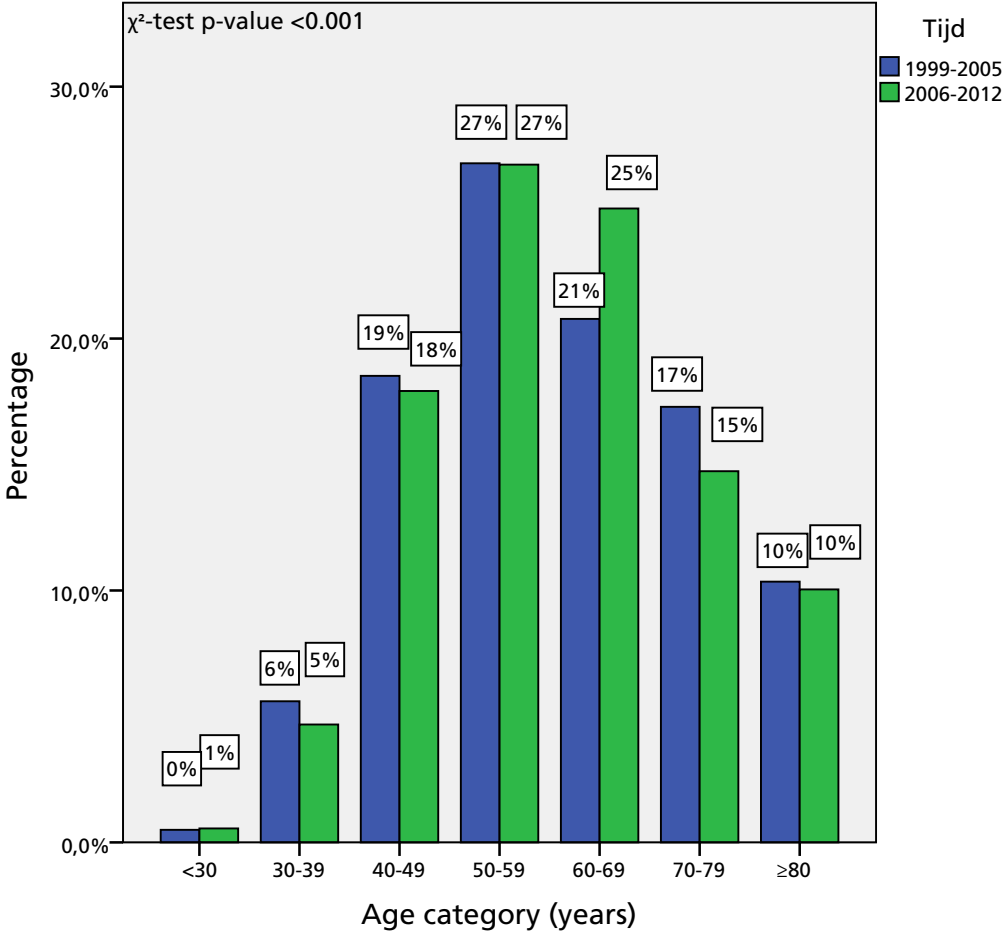# Supplementary figure 1 Age distribution at breast cancer diagnosis in the Netherlands Cancer Registry from 1999-2012

Supplementary table 1 Cox multivariable analyses of clinicopathological variables for 5-years overall mortality in breast cancer patients in the Netherlands Cancer Registry from 1999-2005 and 2006-2012

Clinicopathological variables	1999-2005				2006-2012	
	Number	HR (95% CI)	P-value	Number	HR (95% CI)	P-value
Age at diagnosis in years	79,997	1.05 (1.05 to 1.05)	**<0.001**	93,497	1.05 (1.04 to -1.05)	**<0.001**
Pathological tumour category						
Ductal carcinoma in situ	6,752	0.75 (0.62 to 0.90)	**0.002**	10,306	0.58 (0.48 to 0.70)	**<0.001**
T1a	2,393	Ref		3,840	Ref	
T1b	9,589	1.12 (0.94 to 1.32)	0.211	12,207	1.02 (0.86 to 1.22)	0.819
T1c	29,100	1.65 (1.41 to 1.93)	**<0.001**	34,156	1.59 (1.35 to 1.86)	**<0.001**
T2	26,597	2.42 (2.07 to 2.83)	**<0.001**	27,937	2.32 (1.97 to 2.73)	**<0.001**
T3	2,710	3.48 (2.94 to 4.1)	**<0.001**	3,212	3.02 (2.53 to 3.61)	**<0.001**
T4	2,856	3.72 (3.15 to 4.4)	**<0.001**	1,839	3.59 (3.02 to 4.3)	**<0.001**
Pathological node category						
N0	52,015	Ref		63,476	Ref	
N1	19,006	1.53 (1.45 to 1.61)	**<0.001**	21,899	1.26 (1.19 to 1.35)	**<0.001**
N2	5,983	2.83 (2.64 to 3.03)	**<0.001**	5,398	2.39 (2.18 to 2.63)	**<0.001**
N3	2,993	4.6 (4.3 to 5.0)	**<0.001**	2,724	4.1 (3.72 to 4.5)	**<0.001**
B&R grade						
Grade 1	12,883	Ref		18,972	Ref	
Grade 2	28,652	1.25 (1.17 to 1.33)	**<0.001**	35,817	1.26 (1.17 to 1.36)	**<0.001**
Grade 3 (including anaplastic)	23,920	2.02 (1.89 to 2.16)	**<0.001**	27,099	2.08 (1.93 to 2.25)	**<0.001**
Unknown	14,542	1.52 (1.41 to 1.63)	**<0.001**	11,609	1.90 (1.73 to 2.07)	**<0.001**
Morphology						
Ductal carcinoma or ductal mixed	62,296	Ref		75,706	Ref	
Lobular carcinoma	8,124	0.83 (0.78 to 0.88)	**<0.001**	9,127	0.88 (0.83 to 0.94)	**<0.001**
Other	9,577	1.01 (0.96 to 1.06)	0.741	8,664	0.96 (0.90 to 1.02)	0.163
Breast surgery						
Mastectomy	38,040	Ref		38,307	Ref	
Breast conserving therapy	38,638	0.84 (0.79 to 0.89)	**<0.001**	50,313	0.87 (0.81 to 0.94)	**<0.001**
No surgery	3,319	3.72 (3.46 to 4.0)	**<0.001**	4,877	4.4 (4.1 to 4.8)	**<0.001**
Axillary lymph node dissection						
No	34,562	Ref		62478	Ref	
Yes	45,435	0.95 (0.90 to 1.00)	0.060	31019	1.38 (1.29 to 1.48)	**<0.001**
Chemotherapy						
No	55,980	Ref		58690	Ref	
Yes	24,017	1.21 (1.15 to 1.28)	**<0.001**	34807	0.99 (0.92 to 1.06)	0.77
Hormonal therapy						
No	48,712	Ref		48152	Ref	
Yes	31,285	0.62 (0.60 to 0.65)	**<0.001**	45345	0.45 (0.43 to 0.47)	**<0.001**
Targeted therapy†						
No	79,272	Ref		86088	Ref	
Yes	725	0.66 (0.54 to 0.82)	**<0.001**	7409	0.58 (0.53 to 0.64)	**<0.001**

Radiotherapy						
No	33156	Ref		34,422	Ref	
Yes	46841	0.71 (0.68 to 0.75)	**<0.001**	59,075	0.67 (0.63 to 0.72)	**<0.001**
Second primary breast cancer						
No	76811	Ref		90,026	Ref	
Yes	3186	0.94 (0.87 to 1.03)	0.169	3,471	1.02 (0.93 to 1.13)	0.618

*Cox univariable and multivariable proportional hazard models were developed to estimate hazard ratios with 95% confidence intervals (CI) for overall mortality. Follow-up was restricted to a maximum of 5 years. Median follow-up was 5.0 (0-5) years for the 1999-2005 cohort and 3.9 (0-5) years for the 2006-2012 cohort. In multivariable analysis all clinicopathological relevant variables and variables with a *p*-value <0.05 in univariable analysis were included. The assumption of proportional hazards was found to be valid by graphically plotting the log-log survival curves. A two-sided *p*-value ≤0.05 was considered statistically significant. Missing values were analyzed as separate unknown group within the same variable. B&R= Bloom & Richardson, CI= Confidence Interval, HR= Hazard Rate, N0= no pathologically assessed regional lymph nodes with metastasis/isolated tumour cells, N1= metastasis in 1-3 regional lymph nodes, N2= metastasis in 4-9 regional lymph nodes, N3= metastasis in ≥10 regional lymph nodes, Ref= reference category, T1a= ≤0.5 cm (including micro-invasion), T1b= >0.5 cm and ≤1 cm, T1c= >1 cm and ≤ 2 cm, T2= >2 cm and ≤5 cm, T3= >5 cm, T4= any size with direct extension to chest wall and/or to skin.

†Mainly trastuzumab.