

Supplementary Table 1 Age-adjusted and multivariable-adjusted relative hazards of clinical outcomes in all breast cancer (n=2,555) and ER+ breast cancer (n=2,025) according to Ki67 score, Nurses' Health Study, 1976-2006

All breast cancer	Distant recurrence			Breast cancer-specific mortality			Overall mortality		
	Person-years	Recurrences		Person-years	Deaths		Person-years	Deaths	
	41,598	623		40,009	586		40,009	1110	
	Model	HR	p-value ^a	Model	HR	p-value ^a	Model	HR	p-value ^a
Ki67 score ^c	Age-adjusted	1.44 (0.84-2.47)	0.19	Age-adjusted	2.00 (1.17-3.41)	0.01	Age-adjusted	1.32 (0.86-2.01)	0.20
	Multivariable ^b	1.23 (0.69-2.20)	0.49	Multivariable ^b	1.78 (0.99-3.18)	0.05	Multivariable ^b	1.40 (0.89-2.20)	0.15
	MV + grade	1.10 (0.61-1.99)	0.75	MV + grade	1.51 (0.83-2.74)	0.17	MV + grade	1.28 (0.81-2.02)	0.30
Ki67 ≥ 14%	Age-adjusted	1.22 (1.02-1.45)	0.03	Age-adjusted	1.38 (1.15-1.65)	0.0004	Age-adjusted	1.14 (1.00-1.31)	0.06
	Multivariable ^b	1.14 (0.95-1.37)	0.16	Multivariable ^b	1.33 (1.10-1.61)	0.003	Multivariable ^b	1.15 (1.00-1.32)	0.05
	MV + grade	1.10 (0.91-1.32)	0.32	MV + grade	1.26 (1.04-1.52)	0.02	MV + grade	1.12 (0.97-1.29)	0.13
ER+ breast cancer	Person-years	Recurrences		Person-years	Deaths		Person-years	Deaths	
	32,182	438		30,964	409		30,964	829	
	Model	HR	p-value ^a	Model	HR	p-value ^a	Model	HR	p-value ^a
Ki67 score	Age-adjusted	1.87 (0.88-3.93)	0.10	Age-adjusted	2.93 (1.43-6.01)	0.003	Age-adjusted	1.65 (0.94-2.90)	0.08
	Multivariable ^b	1.66 (0.74-3.74)	0.22	Multivariable ^b	2.94 (1.32-6.54)	0.008	Multivariable ^b	1.70 (0.93-3.09)	0.08
	MV + grade	1.56 (0.69-3.56)	0.29	MV + grade	2.75 (1.22-6.21)	0.02	MV + grade	1.63 (0.89-2.99)	0.11
Ki67 ≥ 14%	Age-adjusted	1.23 (0.98-1.54)	0.07	Age-adjusted	1.43 (1.13-1.80)	0.002	Age-adjusted	1.16 (0.98-1.38)	0.08
	Multivariable ^b	1.13 (0.90-1.44)	0.29	Multivariable ^b	1.36 (1.07-1.73)	0.01	Multivariable ^b	1.14 (0.96-1.36)	0.14
	MV + grade	1.10 (0.87-1.39)	0.44	MV + grade	1.29 (1.02-1.65)	0.04	MV + grade	1.12 (0.94-1.33)	0.21

HR hazard ratio

^a χ^2 tests

^b Adjusted for age and breast cancer prognostic factors including menopausal status and MH use (premenopausal, never user, past user, current estrogen user, current estrogen and progesterone user, current other user, unknown status), BMI (<20, 20-21.9, 22-23.9, 24-26.9, 27+ kg/m²), smoking status (never, current and past smoker) weight change at least 12 months after diagnosis (>10% loss, 5-10% loss, <5% loss to <5% gain, 5-10% gain, >10% gain), physical activity at least 24 months after diagnosis (<3, 3-8.9, 9-14.9, 15-23.9, 24+ metabolic equivalents/week), stages I-III, chemotherapy (yes/no), radiation therapy (yes/no), tamoxifen use (yes/no), other hormone therapy (yes/no), date of diagnosis and time since diagnosis.

^c Ki67 score is a continuous score representing the percentage of Ki67 positive nuclei detected by Definiens (0-100%)