

S7 Table. Cox proportional hazards model of survival for patients with and without insulin and/or metformin exposure before the diagnosis of breast cancer

Variables	Univariable analysis Hazard ratio (95% CI)	p-value	Multivariable analysis Hazard ratio (95% CI)	p-value
Histologic type				
IDC	1		1	
ILC	1.785 (0.720-4.426)	0.211	1.453 (0.505-3.463)	0.456
Others	0.266 (0.097-0.728)	0.010	0.326 (0.077-0.922)	0.033
Stage: T				
T1	1		1	
T0	1.319 (0.010-9.686)	0.853	0.654 (0.005-5.949)	0.764
T2	3.195 (1.887-5.670)	< 0.001	2.901 (1.651-5.326)	< 0.001
T3	8.032 (3.943-16.115)	< 0.001	4.557 (1.974-10.512)	< 0.001
T4	3.953 (0.437-15.659)	0.178	1.248 (0.123-6.273)	0.819
Tis	0.768 (0.153-2.441)	0.687	2.608 (0.406-13.784)	0.288
Stage: N				
N0	1		1	
N1	2.010 (1.183-3.414)	0.010	1.379 (0.778-2.427)	0.268
N2	3.585 (1.762-7.294)	< 0.001	2.340 (1.057-4.802)	0.037
N3	8.440 (4.629-15.392)	< 0.001	3.560 (1.682-7.181)	0.001
Stage: M				
M0	1		1	
M1	8.975 (3.276-24.588)	< 0.001	3.477 (1.037-9.339)	0.044
ER				
Negative	1		1	
Positive	0.655 (0.421-1.020)	0.061	1.218 (0.673-2.154)	0.508
PR				

Negative	1		1	
Positive	0.494 (0.315-0.774)	0.002	0.495 (0.282-0.886)	0.019
Age at diagnosis (yr)				
< 40 years old	1		1	
≥ 40 and < 50	0.635 (0.199-2.028)	0.444	0.645 (0.221-2.218)	0.458
≥ 50	1.018 (0.371-2.796)	0.972	0.819 (0.329-2.598)	0.705
CCI	1.152 (1.053-1.261)	0.002	1.085 (0.980-1.199)	0.116
Exposure before breast cancer				
Reference: no exposure to either drug	1		1	
Exposure to insulin	3.704 (1.572-8.730)	0.003	5.714 (2.106-13.424)	0.001
Exposure to metformin	1.178 (0.711-1.951)	0.525	1.006 (0.590-1.683)	0.982
Exposure to insulin and metformin	1.549 (0.796-3.015)	0.198	1.209 (0.581-2.335)	0.595

CCI, Charlson comorbidity index; CI, confidence interval; ER, estrogen receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; M, metastasis; N, node; PR, progesterone receptor; T, tumor.