

SUPPLEMENTARY TABLES

Supplementary Table 1. Association between PAA and breast cancer treatments (N=1,236).

Treatment	N yes/ N no	At diagnosis		Year 1		Year 2		Year 5		Year 10	
		Δ PAA	p	Δ PAA	p	Δ PAA	p	Δ PAA	p	Δ PAA	p
Surgery	1,124 /112	1.9	0.03	0.47	0.549	-2.59	0.001	-5.64	<0.001	-6.91	<0.001
Radiation therapy	639/597	0.79	0.056	0.62	0.083	-0.47	0.174	-1.78	<0.001	-1.86	<0.001
Chemotherapy	759/477	4.83	<0.001	1.81	<0.001	0.84	0.05	0.11	0.79	-0.22	0.647
Hormone therapy	837/399	1.52	0.003	-1.13	0.015	-0.79	0.082	0.11	0.813	1.62	0.001
Targeted therapy	213/1,023	-1.08	0.105	-0.29	0.647	0.01	0.993	-0.08	0.894	0.07	0.923

Difference in PAA estimated using linear mixed models with an interaction between exposures and a natural spline of year since diagnosis, with adjustment for cancer stage, grade, subtype, and mutual adjustment for other treatments.

Supplementary Table 2. Association between PAA and breast cancer treatment pattern (N=1,236).

Treatment	N	At diagnosis		Year 1		Year 2		Year 5		Year 10	
		Δ PAA	p	Δ PAA	p	Δ PAA	p	Δ PAA	p	Δ PAA	p
Surgery only	67	Reference		Reference		Reference		Reference		Reference	
Surgery+radiation	49	-0.41	0.843	0.61	0.726	-0.87	0.561	-2.4	0.077	1.1	0.459
Surgery+chemo	69	5.91	<0.001	4.83	0.001	1.68	0.209	-0.21	0.865	2.44	0.078
Surgery+hormone	140	1.34	0.367	0.44	0.738	-1.6	0.162	-1.83	0.089	3.81	0.002
Surgery+radiation+hormone	186	0.86	0.564	0.51	0.691	-1.32	0.234	-1.14	0.27	3.07	0.007
Surgery+chemo+hormone	142	6.58	<0.001	1.43	0.277	-1.5	0.195	-1.5	0.171	2.66	0.026
Surgery+radiation+chemo	102	3.99	0.01	3.85	0.009	-0.34	0.798	-2.4	0.06	0	0.999
Surgery+radiation+chemo+hormone	185	6.84	<0.001	1.71	0.186	-1.67	0.141	-2.99	0.005	1.09	0.346
Surgery+radiation+chemo+hormone+targeted	66	6.22	<0.001	2.98	0.04	-0.19	0.883	-1.46	0.249	2.77	0.046
Other	230	3.81	0.009	2.14	0.109	0.29	0.806	0.75	0.504	4.97	<0.001

Difference in PAA estimated using linear mixed models with an interaction between exposures and a natural spline of year since diagnosis, with adjustment for cancer stage, grade, and subtype.

Supplementary Table 3. Association between PAA as residuals and clinical characteristics among breast cancer patients (N=1,264).

Clinical characteristics	N	At diagnosis		Year 1		Year 2		Year 5		Year 10	
		Δ PAA	p	Δ PAA	p	Δ PAA	p	Δ PAA	p	Δ PAA	p
Cases vs controls	1,264	2.09	<0.001	0.28	0.423	-0.42	0.092	-0.88	<0.001	0.25	0.373
Age at diagnosis											
<45	247	Reference		Reference		Reference		Reference		Reference	
45-54	383	-0.12	0.714	0.2	0.381	0.31	0.095	-0.02	0.898	-0.6	0.01
55-64	379	-0.69	0.052	-0.66	0.005	-0.14	0.457	0.44	0.012	0.55	0.015
≥65	255	-2.53	<0.001	0.28	0.29	0.66	0.002	0.39	0.089	0.44	0.193
Stage											
0	100	Reference		Reference		Reference		Reference		Reference	
I	447	1.27	0.028	0.92	0.054	-0.41	0.268	-0.68	0.023	-0.21	0.563
II	413	1.94	<0.001	0.92	0.049	-1.01	0.006	-1.76	<0.001	-0.5	0.186
III/IV	216	1.41	0.013	-0.41	0.383	-0.39	0.282	0.64	0.032	0.84	0.037
Grade											
Low	232	Reference		Reference		Reference		Reference		Reference	
Intermediate	499	-0.24	0.561	-0.03	0.906	0.12	0.572	-0.15	0.443	0.11	0.688
High	439	-0.24	0.548	0.4	0.136	0.03	0.876	-0.67	0.001	0.07	0.787
Subtype											
HR+/HER2-	570	Reference		Reference		Reference		Reference		Reference	
HER2+	163	-1.39	<0.001	0.6	0.003	0.84	<0.001	-0.05	0.802	-0.23	0.441
Triple-negative	171	-1.34	<0.001	0.92	<0.001	0.05	0.825	-1.06	<0.001	-1.65	<0.001

Difference in PAA estimated using linear mixed models with an interaction between exposures and a natural spline of year since diagnosis.

Supplementary Table 4. Association between PAA as residuals and breast cancer treatment pattern (N=1,236).

Treatment	N	Year 1		Year 2		Year 5		Year 10	
		Δ PAA	p	Δ PAA	p	Δ PAA	p	Δ PAA	p
Treatment combination¹									
Surgery(+radiation)	116	Reference		Reference		Reference		Reference	
Surgery(+radiation)+chemo	171	1.54	0.02	-0.49	0.329	-0.98	0.023	0.25	0.617
Surgery(+radiation)+endocrine	326	0.31	0.633	-0.81	0.085	-0.31	0.435	1.69	<0.001
Surgery(+radiation)+chemo+endocrine	327	0.6	0.336	-1.29	0.006	-1.23	0.002	0.7	0.117
Surgery(+radiation)+chemo+endocrine +targeted	106	0.8	0.211	-0.88	0.079	-1.11	0.013	0.99	0.085
Other	190	0.58	0.358	-0.3	0.529	0.48	0.234	1.61	0.001
Medication²	N (yes/no)								
Chemotherapy									
Alkylating	634/602	0.81	<0.001	-0.2	0.192	-1.02	<0.001	-0.76	<0.001
Anthracyclines	469/767	0.67	<0.001	-0.17	0.251	-1.38	<0.001	-1.09	<0.001
Antimetabolite	157/1,079	-2.33	<0.001	0.26	0.096	1.62	<0.001	0.8	<0.001
Anti-microtubule/taxane	645/591	-0.05	0.821	-0.46	0.007	-0.46	0.005	-0.23	0.25
Endocrine therapy									
SERM	437/799	-0.35	0.049	-0.31	0.028	-0.38	0.006	0.09	0.645
Aromatase inhibitor	634/602	-0.56	0.001	-0.63	<0.001	0	0.975	0.84	<0.001

¹Difference in PAA estimated using linear mixed models with an interaction between exposures and a natural spline of year since diagnosis, with adjustment for cancer stage, grade, and subtype; ²Difference in PAA estimated using linear mixed models with an interaction between exposures and a natural spline of year since diagnosis, with adjustment for cancer stage, grade, subtype, other treatments, and other drugs of the treatment type.