Supplementary Online Content

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eTable 1. Select Characteristics of 7,541 Kaiser Permanente Breast Cancer Patients, by Occurrence of Second Contralateral Breast Cancer (CBC)

eTable 2. Association of Select Characteristics of 7,541 Kaiser Permanente Breast Cancer Patients With Ever Use of Adjuvant Tamoxifen Therapy

eTable 3. Multivariate Relative Risks (RR) and 95% Confidence Intervals (CI) for Contralateral Breast Cancer Associated With Adjuvant Tamoxifen Therapy of Varying Durations and Times Since Last Use

eTable 4. Multivariate Relative Risks (RR) and 95% Confidence Intervals (CI) for Contralateral Breast Cancer Associated With Adjuvant Tamoxifen Therapy by Age at Diagnosis of the Initial Breast Cancer

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Select Characteristics of 7,541 Kaiser Permanente Breast Cancer Patients, by Occurrence of Second Contralateral Breast Cancer (CBC)

Patient Characteristics	Non-cases N	Non-cases Column %*	CBC cases N	CBC cases Column %
Total	**7293**	**100.0**	**248**	**100.0**
Kaiser Center				
Colorado	3197	43.8	78	31.5
Northwest	4096	56.2	170	68.6
Year of Initial BC Diagnosis				
1990-1994	1066	14.6	66	26.6
1995-1999	2092	28.7	96	38.7
2000-2004	2228	30.6	65	26.2
2005-2008	1907	26.2	21	8.5
Age at Initial BC Diagnosis (years)				
24-39	260	3.6	13	5.2
40-49	1236	17.0	40	16.1
50-59	2003	27.5	67	27.0
60-69	1991	27.3	76	30.7
70-79	1406	19.3	41	16.5
80+	397	5.4	11	4.4
Race				
White	6777	92.9	232	93.6
Black	194	2.7	8	3.2
Other	322	4.4	8	3.2
Stage of Initial BC Diagnosis				
I	4364	59.8	157	63.3
II	2420	33.2	79	31.9
III	476	6.5	12	4.8
Unknown	33	0.5	0	0.0
Grade of Initial BC Diagnosis				
Well differentiated	2105	28.9	60	24.2
Moderately differentiated	2675	36.7	78	31.5
Poorly differentiated	1727	23.7	54	21.8
Undifferentiated, anaplastic	26	0.4	2	0.8
Grade or differentiation not determined	760	10.4	54	21.8

Histology of Initial BC Diagnosis				
Infiltrating ductal	5613	77.0	185	74.6
Lobular	599	8.2	20	8.1
Mixed	473	6.5	20	8.1
All others	608	8.3	23	9.3
Estrogen Receptor Status of Initial BC Diagnosis				
Positive	5760	79.0	191	77.0
Negative	1193	16.4	43	17.3
Unknown, borderline	340	4.7	14	5.7
BC Radiotherapy for Initial Diagnosis				
No	2382	32.7	76	30.7
Yes	4911	67.3	172	69.4
BC Initial Chemotherapy with Alkylating Agents				
No	4852	66.5	162	65.3
Yes	2441	33.5	86	34.7
BC Type of Adjuvant Endocrine Therapy*				
No hormonal therapy	2531	34.7	121	48.8
Tamoxifen, no AI	2833	38.9	101	40.7
AI, no tamoxifen	953	13.1	10	4.0
Tamoxifen and AI	950	13.0	16	6.5
Other endocrine therapy	26	0.0	0	0.0
BC Recurrence ‡				
No	6588	90.3	243	98.0
Yes	705	9.7	5	2.0
Years of Follow-up†				
<2 yrs	1224	16.8	59	23.8
2-<5 yrs	2205	30.2	66	26.6
5-<10 yrs	2259	31.0	92	37.1
10-<15 yrs	1227	16.8	24	9.7
15+	378	5.2	7	2.8

AI, aromatase inhibitor; BC, breast cancer; CBC, contralateral breast cancer. Column percentages may not sum to 100% due to rounding.

* Adjuvant endocrine therapy use was defined as therapy of 90 days or more during any one treament course at any time during follow-up (entry date to exit date).

‡ BC recurrence includes regional or metastatic recurrence or type of recurrence not reported. (i.e., excludes localized recurrence only)

† Entry date (BC diagnosis plus 12 months) to exit date.

eTable 2. Association of Select Characteristics of 7,541 Kaiser Permanente Breast Cancer Patients With Ever Use of Adjuvant Tamoxifen Therapy

| Patient Characteristics | Adjuvant Tamoxifen Therapy* | | | | OR [#] | 95% CI | | |
| | No | | Yes | | | | | |
	N	Row %	N	Row %				
Total	3641	48.3	3900	51.7				
Kaiser Center								
Colorado	1564	47.8	1711	52.2	REF			
Northwest	2077	48.7	2189	51.3	0.81	0.73	to	0.90
Year of Initial BC Diagnosis								
1990-1994	445	39.3	687	60.7	REF			
1995-1999	872	39.9	1316	60.2	0.90	0.75	to	1.09
2000-2004	1048	45.7	1245	54.3	0.63	0.52	to	0.76
2005-2008	1276	66.2	652	33.8	0.22	0.18	to	0.27
Age at Initial BC Diagnosis (years)								
24-39	150	55.0	123	45.1	REF			
40-49	529	41.5	747	58.5	1.53	1.12	to	2.08
50-59	1006	48.6	1064	51.4	1.14	0.84	to	1.53
60-69	1024	49.5	1043	50.5	1.00	0.73	to	1.35
70-79	700	48.4	747	51.6	1.02	0.75	to	1.40
80+	232	56.9	176	43.1	0.74	0.51	to	1.06
Race								
White	3314	47.3	3695	52.7	REF			
Black	130	64.4	72	35.6	0.57	0.41	to	0.80
Other	197	59.7	133	40.3	0.68	0.53	to	0.87
Stage of Initial BC Diagnosis								
I	2294	50.7	2227	49.3	REF			
II	1071	42.9	1428	57.1	1.64	1.44	to	1.87
III	256	52.5	232	47.5	1.38	1.09	to	1.75
Unknown	20	60.6	13	39.4	0.93	0.41	to	2.11
Grade of Initial BC Diagnosis								
Well differentiated	998	46.1	1167	53.9	REF			
Moderately differentiated	1146	41.6	1607	58.4	1.21	1.06	to	1.37
Poorly differentiated	1124	63.1	657	36.9	0.87	0.74	to	1.03
Undifferentiated, anaplastic	19	67.9	9	32.1	1.11	0.44	to	2.79

	N	%	N	%	OR	95% CI		
Grade or differentiation not determined	354	43.5	460	56.5	1.02	0.83	to	1.26
Estrogen Receptor Status of Initial BC Diagnosis								
Positive	2352	39.5	3599	60.5	REF			
Negative	1070	86.6	166	13.4	0.08	0.06	to	0.09
Unknown, borderline	219	61.9	135	38.1	0.32	0.25	to	0.40
BC Radiotherapy for Initial Diagnosis								
No	1189	48.4	1269	51.6	REF			
Yes	2452	48.2	2631	51.8	1.10	0.98	to	1.23
BC Initial Chemotherapy with Alkylating Agents								
No	2378	47.4	2636	52.6	REF			
Yes	1263	50.0	1264	50.0	1.22	1.05	to	1.41
BC Recurrence ‡								
No	3337	48.9	3494	51.2	N/A			
Yes	304	42.8	406	57.2				

Abbreviations: BC, breast cancer; CI, confidence interval; OR, odds ratio.

* Adjuvant tamoxifen therapy use was defined as therapy of 90 days or more during any one treatment course at any time during follow-up (entry date to exit date).

‡ BC recurrence includes regional or metastatic recurrence or type of recurrence not reported. (i.e., excludes localized recurrence only)

OR (95% CI) of relation between patient characteristics and tamoxifen use was mutually adjusted for all other factors shown in this table, except BC recurrence.

eTable 3. Multivariate* Relative Risks (RR) and 95% Confidence Intervals (CI) for Contralateral Breast Cancer Associated With Adjuvant Tamoxifen Therapy of Varying Durations and Times Since Last Use

Time since last tamoxifen use and duration of therapy	No. CBC	Person-years	RR	95% CI
Never used or used for <90 days	131	20760	REF	
Current user				
Duration 90 days-<1 year	6	1717	0.71	0.26 to 1.70
Duration 1-<4 years	24	8053	**0.49**	**0.29 to 0.82**
Duration 4+ years	3	1429	**0.26**	**0.06 to 0.76**
Former user, 30days-<3y since last use				
Duration 90 days-<1 year	6	1175	0.94	0.35 to 2.13
Duration 1-<4 years	12	2949	0.54	0.26 to 1.03
Duration 4+ years	14	3427	**0.42**	**0.21 to 0.78**
Former user, 3-<5y since last use				
Duration 90 days-<1 year	6	481	2.14	0.79 to 4.83
Duration 1-<4 years	13	1252	1.04	0.51 to 1.98
Duration 4+ years	6	1653	**0.23**	**0.08 to 0.55**
Former user, 5+y since last use				
Duration 90 days-<1 year	6	897	0.61	0.23 to 1.37
Duration 1-<4 years	12	2043	0.62	0.29 to 1.22
Duration 4+ years	9	2138	0.49	0.20 to 1.08

CI, confidence interval; CBC, contralateral breast cancer; REF, referent group; RR, relative risk.
* Poisson models were stratified by study site (NW/CO), age at diagnosis (<40, 40-49, 50- 59, 60-69, 70+ years), stage at diagnosis (I, II, III, unknown stage), ER status of the initial tumor (positive, negative, unknown/indeterminate), time since initial breast cancer in yearly categories and 15+ years, and year of diagnosis (1990-94, 1995-99, 2000-04, 2005-2008). We simultaneously adjusted for aromatase inhibitor use (with or without tamoxifen), chemotherapy with an alkylating agent, and radiotherapy

eTable 4. Multivariate* Relative Risks (RR) and 95% Confidence Intervals (CI) for Contralateral Breast Cancer Associated With Adjuvant Tamoxifen Therapy by Age at Diagnosis of the Initial Breast Cancer

Treatment	< 50 years old at intial BC diagnosis				50+ years old at intial BC diagnosis			
	No. CBC	Person-years	RR/y use†	95% CI	No. CBC	Person-years	RR/y use†	95% CI
Tamoxifen duration (years, continuous) and time since last use:								
Never used or used for <90 days	28	4255	REF		103	16505	REF	
Current user	8	2423	0.79	0.47 to 1.18	25	8776	**0.76**	**0.64 to 0.90**
Former user, 30days-<3y since last use	5	1570	0.83	0.55 to 1.15	27	5981	**0.84**	**0.74 to 0.96**
Former use, 3-<5y since last use	5	630	0.74	0.51 to 1.02	20	2756	0.91	0.77 to 1.06
Former user, 5+y since last use	7	1048	0.98	0.68 to 1.35	20	4030	**0.82**	**0.67 to 0.98**

BC, breast cancer; CI, confidence interval; CBC, contralateral breast cancer; REF, referent group; RR, relative risk.

* Poisson models were stratified by study site (NW/CO), age at diagnosis (<40, 40-49, 50-59, 60-69, 70+ years), stage at diagnosis (I, II, III, unknown stage), ER status of the initial tumor (positive, negative, unknown/indeterminate), time since initial breast cancer in yearly categories and 15+ years, and year of diagnosis (1990-94, 1995-99, 2000-04, 2005-2008). We simultaneously adjusted for aromatase inhibitor use (with or without tamoxifen), chemotherapy with an alkylating agent, and radiotherapy.

† RRs from tamoxifen duration trend analyses are estimates of risk per year of tamoxifen use.