

**Appendix 2: Supplementary tables [posted as supplied by author]**

**Table A: Distribution of patient characteristics at baseline pooled across databases**

Patient characteristics	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10)*		Unmatched		Matched (1:10)*	
	CYP2D6-inhibiting SSRIs n=2268	Other SSRIs n=3799	CYP2D6-inhibiting SSRIs n=2026	SSRIs n=2026 out of 3774	CYP2D6-inhibiting SSRIs n=3531	Other SSRIs n=4934	CYP2D6-inhibiting SSRIs n=3025	Other SSRIs n=3025 out of 4768
Database, n (%)								
MAX	1080 (47.6)	1253 (33.0)	911 (45.0)	911 (45.0)	1804 (51.1)	1825 (37.0)	1444 (47.7)	1444 (47.7)
PAAD	117 (5.2)	125 (3.3)	79 (3.9)	79 (3.9)	135 (3.8)	136 (2.8)	93 (3.1)	93 (3.1)
PACE	267 (11.8)	381 (10.0)	249 (12.3)	249 (12.3)	241 (6.8)	238 (4.8)	174 (5.8)	174 (5.8)
Optum	745 (32.8)	1899 (50.0)	740 (36.5)	740 (36.5)	1224 (34.7)	2529 (51.3)	1209 (40.0)	1209 (40.0)
Caremark	59 (2.6)	141 (3.7)	47 (2.3)	47 (2.3)	127 (3.6)	206 (4.2)	105 (3.5)	105 (3.5)
<b>Demographics</b>								
Age, mean (±SD)	57 (±14)	55 (±14)	57 (±14)	56 (±14)	55 (±13)	54 (±13)	55 (±13)	54 (±13)
Index year, n (%)								
1995-1999	250 (11.0)	292 (7.7)	214 (10.6)	210 (10.4)	207 (5.9)	189 (3.8)	148 (4.9)	151 (5.0)
2000-2004	1402 (61.8)	1717 (45.2)	1227 (60.6)	1202 (59.3)	2239 (63.4)	2226 (45.1)	1847 (60.6)	1831 (60.0)
2005-2009	504 (22.2)	1224 (32.2)	473 (23.3)	504 (24.9)	857 (24.3)	1713 (34.7)	822 (27.0)	820 (26.9)
2010-2013	112 (4.9)	566 (14.9)	112 (5.5)	110 (5.4)	228 (6.5)	806 (16.3)	233 (7.6)	248 (8.1)
<b>Breast cancer characteristics</b>								
Breast cancer, n (%)	1152 (50.8)	2172 (57.2)	1034 (51.0)	1027 (50.7)	1783 (50.5)	2727 (55.3)	1559 (51.1)	1561 (51.2)
Breast cancer site, n (%)								
Nipple and areola	137 (6.0)	229 (6.0)	115 (5.7)	123 (6.1)	166 (4.7)	224 (4.5)	136 (4.5)	146 (4.8)
Central	249 (11.0)	514 (13.5)	225 (11.1)	236 (11.6)	335 (9.5)	535 (10.8)	288 (9.4)	287 (9.4)
Upper-inner	173 (7.6)	375 (9.9)	153 (7.6)	155 (7.7)	225 (6.4)	439 (8.9)	199 (6.5)	208 (6.8)
Lower-inner	116 (5.1)	218 (5.7)	100 (4.9)	103 (5.1)	154 (4.4)	252 (5.1)	134 (4.4)	131 (4.3)
Upper-outer	701 (30.9)	1344 (35.4)	624 (30.8)	624 (30.8)	921 (26.1)	1508 (30.6)	802 (26.3)	824 (27.0)
Lower-outer	151 (6.7)	313 (8.2)	126 (6.2)	132 (6.5)	204 (5.8)	361 (7.3)	181 (5.9)	175 (5.7)
Auxiliary tail	30 (1.3)	70 (1.8)	22 (1.1)	24 (1.2)	51 (1.4)	78 (1.6)	45 (1.5)	46 (1.5)
Other/Unspecified	1786 (78.7)	3155 (83.0)	1589 (78.4)	1591 (78.5)	2428 (68.8)	3602 (73.0)	2090 (68.5)	2095 (68.7)
Breast cancer stage any time prior to SSRI, n (%) <sup>†</sup>								
0	632 (27.9)	1370 (36.1)	574 (28.3)	605 (29.9)	938 (26.6)	1585 (32.1)	826 (27.1)	839 (27.5)
I	614 (27.1)	1335 (35.1)	557 (27.5)	589 (29.1)	884 (25.0)	1498 (30.4)	783 (25.7)	794 (26.0)
II	122 (5.4)	253 (6.7)	105 (5.2)	110 (5.4)	157 (4.4)	320 (6.5)	139 (4.6)	146 (4.8)

Patient characteristics	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10)*		Unmatched		Matched (1:10)*	
	CYP2D6-inhibiting SSRIs n=2268	Other SSRIs n=3799	CYP2D6-inhibiting SSRIs n=2026	SSRIs n=2026 out of 3774	CYP2D6-inhibiting SSRIs n=3531	Other SSRIs n=4934	CYP2D6-inhibiting SSRIs n=3025	Other SSRIs n=3025 out of 4768
<b><u>Prior breast cancer screening and treatments</u></b>								
Chemotherapy, n (%)	322 (14.2)	678 (17.8)	294 (14.5)	296 (14.6)	522 (14.8)	895 (18.1)	455 (14.9)	458 (15.0)
Mammography, n (%)	792 (34.9)	1734 (45.6)	715 (35.3)	740 (36.5)	1266 (35.9)	2278 (46.2)	1129 (37.0)	1114 (36.5)
Mastectomy, n (%)	937 (41.3)	1930 (50.8)	841 (41.5)	844 (41.7)	1154 (32.7)	1828 (37.0)	997 (32.7)	997 (32.7)
Radiation, n (%)	666 (29.4)	1268 (33.4)	586 (28.9)	601 (29.7)	725 (20.5)	1233 (25.0)	641 (21.0)	642 (21.0)
<b><u>Medication utilization</u></b>								
Pre-SSRI tamoxifen total days of supply, mean (±SD)	150 (±220)	168 (±245)	150 (±217)	152 (±223)	-	-	-	-
Pre-tamoxifen SSRI days of supply, mean (±SD)					8 (±7)	8 (±6)	2 (±2)	2 (±2)
Number of generics, mean (±SD)	11 (±8)	11 (±8)	11 (±8)	11 (±8)	8 (±7)	8 (±6)	8 (±7)	8 (±6)
Vaccine, n (%)	237 (10.4)	501 (13.2)	212 (10.5)	235 (11.6)	211 (6.0)	371 (7.5)	196 (6.4)	174 (5.7)
Anticoagulants, n (%)	152 (6.7)	286 (7.5)	142 (7.0)	127 (6.3)	212 (6.0)	308 (6.2)	184 (6.0)	185 (6.1)
Antiplatelets, n (%)	43 (1.9)	77 (2.0)	40 (2.0)	38 (1.9)	45 (1.3)	70 (1.4)	38 (1.2)	34 (1.1)
Antipsychotics, n (%)	190 (8.4)	272 (7.2)	166 (8.2)	178 (8.8)	364 (10.3)	472 (9.6)	316 (10.4)	327 (10.7)
Angiotensin converting enzyme-inhibitors, n (%)	382 (16.8)	544 (14.3)	333 (16.4)	344 (17.0)	551 (15.6)	630 (12.8)	452 (14.8)	425 (13.9)
Angiotensin receptor blockers, n (%)	171 (7.5)	326 (8.6)	152 (7.5)	161 (7.9)	225 (6.4)	332 (6.7)	200 (6.6)	202 (6.6)
Beta-blockers, n (%)	419 (18.5)	640 (16.8)	368 (18.2)	343 (16.9)	539 (15.3)	710 (14.4)	470 (15.4)	450 (14.8)
Calcium channel blockers, n (%)	357 (15.7)	548 (14.4)	310 (15.3)	304 (15.0)	497 (14.1)	520 (10.5)	378 (12.4)	371 (12.2)
Diuretics, n (%)	404 (17.8)	616 (16.2)	339 (16.7)	334 (16.5)	566 (16.0)	665 (13.5)	463 (15.2)	447 (14.7)
Statins, n (%)	331 (14.6)	587 (15.5)	298 (14.7)	290 (14.3)	544 (15.4)	762 (15.4)	474 (15.5)	458 (15.0)
Antidepressants drugs, n (%)	1034 (45.6)	1683 (44.3)	895 (44.2)	876 (43.2)	798 (22.6)	1068 (21.6)	682 (22.4)	653 (21.4)
Benzodiazepines, n (%)	942 (41.5)	1655 (43.6)	822 (40.6)	826 (40.8)	1275 (36.1)	1850 (37.5)	1073 (35.2)	1080 (35.4)
Bisphosphonates, n (%)	130 (5.7)	259 (6.8)	110 (5.4)	112 (5.5)	167 (4.7)	200 (4.1)	129 (4.2)	130 (4.3)
CYP2D6 enzyme Inductors, n (%)	265 (11.7)	531 (14.0)	245 (12.1)	234 (11.5)	378 (10.7)	690 (14.0)	345 (11.3)	351 (11.5)
CYP2D6 enzyme Inhibitors, n (%)	816 (36.0)	1015 (26.7)	676 (33.4)	673 (33.2)	400 (11.3)	674 (13.7)	356 (11.7)	341 (11.2)
Estrogens/hormone therapy, n (%)	261 (11.5)	390 (10.3)	215 (10.6)	214 (10.6)	338 (9.6)	460 (9.3)	274 (9.0)	271 (8.9)

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10)*		Unmatched		Matched (1:10)*	
<b>Patient characteristics</b>	CYP2D6-inhibiting SSRIs n=2268	Other SSRIs n=3799	CYP2D6-inhibiting SSRIs n=2026	SSRIs n=2026 out of 3774	CYP2D6-inhibiting SSRIs n=3531	Other SSRIs n=4934	CYP2D6-inhibiting SSRIs n=3025	Other SSRIs n=3025 out of 4768
<b><u>Healthcare utilization</u></b>								
Hospital admission, n (%)	688 (30.3)	1158 (30.5)	605 (29.9)	600 (29.6)	755 (21.4)	1083 (21.9)	640 (21.0)	637 (20.9)
Number of days hospitalized, mean (±SD)	2 (±6)	2 (±8)	2 (±6)	2 (±7)	2 (±5)	2 (±7)	2 (±6)	2 (±6)
Number of Medical Practitioner visits, mean (±SD)	11 (±12)	13 (±13)	11 (±12)	11 (±12)	6 (±6)	7 (±7)	6 (±6)	6 (±6)
Combined comorbidity score, mean (±SD)	2 (±3)	2 (±3)	2 (±3)	2 (±3)	2 (±2)	2 (±2)	2 (±2)	2 (±2)

\* Patients with a CYP2D6-inhibiting SSRI were matched on the propensity score to at least 1 and at most 10 patients with another SSRI. A random patient in the other SSRI group was drawn from each matched set to show covariate balance resulting from the matching process.

Cohort 1: Patients were exposed to tamoxifen prior to initiating an SSRI.

Cohort 2: Patients were exposed to an SSRI prior to initiating tamoxifen.

† Data for stages III and IV breast cancer are suppressed in accordance with CMS's current cell size suppression policy, which stipulates that no cell (e.g. admissions, discharges, patients, services) 10 or less may be displayed.

**Caremark**, Medicare data linked to pharmacy claims data from CVS Caremark (2005-2008); **MAX**, Medicaid Analytic Extract (2001-2006); **PAAD**, and the New Jersey Pharmaceutical Assistance to the Aged and Disabled (1995-2005); **PACE**, the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (1995-2005); **Optum Research Database** (2004-2013), comprises data on approximately 40 million UnitedHealth enrollees.

**Table B:** Effects estimate among patient population prior to propensity score matching

Study design	Deaths/Total	HR	95%	95%	P
			LCL	UCL	
<b>Primary analysis</b>					
Pooled databases (Cohort 1)	1054/ 6183	0.98	0.87	1.11	0.79
Pooled databases (Cohort 2)	1146/ 8798	1.08	0.96	1.22	0.19
Overall population (Cohorts 1 and 2)	2200/ 14981	0.96	0.86	1.07	0.43
<b>Sensitivity analyses:<sup>a</sup></b>					
<b>As-treated analysis*</b>					
Pooled databases (Cohort 1)	41/ 6183	0.85	0.45	1.62	0.63
Pooled databases (Cohort 2)	84/ 8798	1.24	0.81	1.91	0.32
Overall population (Cohorts 1 and 2)	125/ 14981	0.92	0.64	1.32	0.65
<b>Patients with pre-existing breast cancer diagnosis (stages I-IV only)</b>					
Pooled databases (Cohort 1)	379/ 1915	1.07	0.87	1.31	0.53
Pooled databases (Cohort 2)	402/ 2732	1.16	0.95	1.41	0.14
Overall population (Cohorts 1 and 2)	781/ 4647	0.97	0.79	1.20	0.81

**Table C:** All-cause mortality associated with concomitant use of tamoxifen and CYP2D6-inhibiting selective serotonin reuptake inhibitors (SSRIs) vs. tamoxifen and other SSRIs in as-treated analyses.

Database	Deaths/Total	Hazard ratio	95% confidence interval	
			Lower	Upper
<b>Cohort 1</b>				
Caremark	* / 174	0.00	0.00	0.00
MAX	13 / 2112	0.43	0.12	1.62
PACE	18 / 624	0.79	0.30	2.06
PAAD	*/ 201	0.50	0.04	5.69
Optum	* / 2638	0.54	0.05	6.19
<b>Pooled databases (Cohort 1)</b>	<b>39 / 5749</b>	<b>0.63</b>	<b>0.31</b>	<b>1.28</b>
<b>Cohort 2</b>				
Caremark	11 / 307	1.51	0.43	5.32
MAX	31 / 3113	0.96	0.47	1.96
PACE	19 / 410	1.19	0.47	3.01
PAAD	8 / 226	1.81	0.40	8.10
Optum	10 / 3737	0.91	0.22	3.7
<b>Pooled databases (Cohort 2)</b>	<b>79 / 7793</b>	<b>1.12</b>	<b>0.71</b>	<b>1.78</b>
<b>Pooled databases (Cohorts 1 and 2 combined)</b>	<b>118 / 13628</b>	<b>0.99</b>	<b>0.67</b>	<b>1.46</b>

\*Data suppressed according to CMS's current cell size suppression policy, which stipulates that no cell (e.g. admissions, discharges, patients, services) 10 or less may be displayed.

**Caremark**, Medicare data linked to pharmacy claims data from CVS Caremark (2005-2008); **MAX**, Medicaid Analytic eXtract (2001-2006); **PAAD**, and the New Jersey Pharmaceutical Assistance to the Aged and Disabled (1995-2005); **PACE**, the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (1995-2005); **Optum Research Database** (2004-2013), comprises data on approximately 40 million UnitedHealth enrollees.

**Table D:** All-cause mortality associated with concomitant use of tamoxifen and CYP2D6-inhibiting selective serotonin reuptake inhibitors (SSRIs) vs. tamoxifen and other SSRIs among only patients with a breast cancer diagnosis in the baseline period.

Database	Deaths/Total	Hazard ratio	95% confidence interval	
			Lower	Upper
<b>Main analysis</b>				
Pooled databases (Cohort 1)	429 / 3071	0.99	0.81	1.21
Pooled databases (Cohort 2)	460 / 4199	1.07	0.88	1.31
<b>All tamoxifen users (Cohorts 1 and 2)</b>	<b>889 / 7270</b>	<b>1.03</b>	<b>0.89</b>	<b>1.18</b>
<b>As-treated analysis</b>				
Pooled databases (Cohort 1)	20 / 3071	0.68	0.26	1.82
Pooled databases (Cohort 2)	37 / 4199	0.95	0.47	1.89
<b>All tamoxifen users (Cohorts 1 and 2)</b>	<b>57 / 7270</b>	<b>0.77</b>	<b>0.44</b>	<b>1.38</b>
<b>Duration of concomitant exposure to tamoxifen and SSRIs</b>				
30 days	704/ 5922	1.08	0.92	1.27
60 days	415/ 3719	0.97	0.78	1.20
90 days	305/ 2816	0.93	0.73	1.19
120 days	264/ 2100	1.07	0.81	1.42
180 days	177/ 1428	1.30	0.93	1.83
240 days	128/ 987	1.36	0.90	2.06

**Table E:** Risk of all-cause mortality associated with concomitant use of tamoxifen and CYP2D6-inhibiting selective serotonin reuptake inhibitors (SSRIs) vs. tamoxifen and other SSRIs in sensitivity analyses.

Study design	Deaths	Person-years	Rate**	Deaths	Person-years	Rate**	HR (95% CI)
	Tamoxifen plus potent CYP2D6-inhibiting SSRIs			Tamoxifen plus other SSRIs			
<b>Primary analysis</b>							
Pooled databases (Cohort 1)	610	9524	64.1	381	5895	64.6	0.91 (0.80 to 1.04)
Pooled databases (Cohort 2)	407	7541	54.0	607	11488	52.8	1.02 (0.89 to 1.16)
Overall population (Cohorts 1 and 2)	788	13436	58.7	1217	21013	57.9	0.96 (0.88 to 1.06)
<b>Sensitivity analyses:<sup>a</sup></b>							
<b>As-treated analysis*</b>							
Pooled databases (Cohort 1)	26	1127	19.2	12	624	23.1	0.68 (0.34 to 1.38)
Pooled databases (Cohort 2)	35	1179	29.7	44	1775	24.8	1.19 (0.75 to 1.89)
Overall population (Cohorts 1 and 2)	62	3022	20.5	94	4709	20.0	0.99 (0.67 to 1.46)
<b>Patients with pre-existing breast cancer diagnosis (stages 0-IV)</b>							
Pooled databases (Cohort 1)	161	2587	62.2	268	4984	53.8	0.99 (0.81 to 1.21)
Pooled databases (Cohort 2)	182	3630	50.1	278	6150	45.2	1.07 (0.88 to 1.31)
Overall population (Cohorts 1 and 2)	343	6217	55.2	546	11133	49.0	1.03 (0.89 to 1.18)
<b>Patients with pre-existing breast cancer diagnosis (stages I-IV only)</b>							
Pooled databases (Cohort 1)	268	4984	53.8	192	2778	69.1	0.95 (0.75 to 1.21)
Pooled databases (Cohort 2)	141	2339	60.3	205	3720	55.1	1.07 (0.85 to 1.33)
Overall population (Cohorts 1 and 2)	546	11133	49.0	397	6498	61.1	1.04 (0.86 to 1.26)
<b>Paroxetine use versus other SSRIs<sup>†</sup></b>							
Pooled databases (Cohort 1)	92	2574	35.8	220	6753	32.6	1.03 (0.80 to 1.33)
Pooled databases (Cohort 2)	124	3931	31.6	342	9741	35.1	0.89 (0.72 to 1.11)
Overall population (Cohorts 1 and 2)	92	2574	35.8	220	6753	32.6	0.95 (0.81 to 1.12)
<b>Fluoxetine use versus other SSRIs<sup>††</sup></b>							
Pooled databases (Cohort 1)	53	1882	28.2	231	7298	31.7	0.99 (0.73 to 1.34)
Pooled databases (Cohort 2)	109	3156	34.5	349	10022	34.8	1.05 (0.85 to 1.31)
Overall population (Cohorts 1 and 2)	162	5038	32.2	580	17320	33.5	1.04 (0.87 to 1.25)

**Table F: Distribution of patient characteristics at baseline from Caremark database**

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=59	Other SSRIs n=141	CYP2D6-inhibiting SSRIs n=47	Other SSRIs n=47 of 127 matched	CYP2D6-inhibiting SSRIs n=127	Other SSRIs n=206	CYP2D6-inhibiting SSRIs n=105	Other SSRIs n=105 of 202 matched
<b>Demographics</b>								
Age, mean (±SD)	75 (±8)	77 (±8)	76 (±7)	77 (±7)	75 (±7)	76 (±8)	76 (±7)	75 (±8)
Index year, n (%)								
2005	20 (33.9)	53 (37.6)	18 (38.3)	18 (38.3)	61 (48.0)	80 (38.8)	48 (45.7)	51 (48.6)
2006	12 (20.3)	33 (23.4)	*	11 (23.4)	21 (16.5)	25 (12.1)	17 (16.2)	14 (13.3)
2007	*	20 (14.2)	*	*	16 (12.6)	32 (15.5)	15 (14.3)	13 (12.4)
2008	20 (33.9)	35 (24.8)	14 (29.8)	14 (29.8)	29 (22.8)	69 (33.5)	25 (23.8)	27 (25.7)
<b>Comorbidities</b>								
Breast cancer, n (%)	17 (28.8)	40 (28.4)	11 (23.4)	*	38 (29.9)	70 (34.0)	33 (31.4)	35 (33.3)
Breast cancer site, n (%)								
Nipple and areola	*	*	*	*	*	*	*	*
Central	*	13 (9.2)	*	*	14 (11.0)	*	*	*
Upper-inner	*	*	*	*	*	*	*	*
Lower-inner	*	*	*	47 (100.0)	*	*	*	*
Upper-outer	15 (25.4)	41 (29.1)	11 (23.4)	*	21 (16.5)	39 (18.9)	19 (18.1)	18 (17.1)
Lower-outer	*	*	*	*	*	*	*	*
Auxiliary tail	*	*	*	*	*	*	*	*
Other/Unspecified	44 (74.6)	118 (83.7)	34 (72.3)	37 (78.7)	85 (66.9)	132 (64.1)	66 (62.9)	65 (61.9)
Breast cancer stage any time prior to SSRI, n (%)								
0	*	30 (21.3)	*	*	24 (18.9)	47 (22.8)	19 (18.1)	22 (21.0)
I	*	30 (21.3)	*	*	23 (18.1)	40 (19.4)	18 (17.1)	18 (17.1)
II	*	*	*	47 (100.0)	*	*	*	*
III	*	141 (100.0)	*	47 (100.0)	*	*	*	*
IV	*	141 (100.0)	*	47 (100.0)	*	*	*	*
<b>Procedures</b>								
Chemotherapy, n (%)	*	*	*	*	*	*	*	*
Mammography, n (%)	29 (49.2)	79 (56.0)	20 (42.6)	22 (46.8)	59 (46.5)	98 (47.6)	49 (46.7)	48 (45.7)
Mastectomy, n (%)	16 (27.1)	33 (23.4)	*	*	30 (23.6)	37 (18.0)	20 (19.0)	23 (21.9)
Radiation, n (%)	16 (27.1)	21 (14.9)	*	11 (23.4)	17 (13.4)	27 (13.1)	13 (12.4)	11 (10.5)
<b>Medication utilization</b>								
Pre-SSRI tamoxifen total days of supply, mean (±SD)	95 (±95)	118 (±130)	100 (±101)	109 (±107)	-	-	-	-
Pre-tamoxifen SSRI days of supply, mean (±SD)	-	-	-	-	17 (±23)	15 (±19)	19 (±24)	17 (±21)

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRI n=59	Other SSRI n=141	CYP2D6-inhibiting SSRI n=47	Other SSRI n=47 of 127 matched	CYP2D6-inhibiting SSRI n=127	Other SSRI n=206	CYP2D6-inhibiting SSRI n=105	Other SSRI n=105 of 202 matched
Number of generics, mean (±SD)	*	*	*	*	*	*	*	*
Vaccine, n (%)	13 (22.0)	36 (25.5)	*	12 (25.5)	15 (11.8)	20 (9.7)	*	*
Anticoagulants, n (%)	*	14 (9.9)	*	*	11 (8.7)	17 (8.3)	*	*
Antiplatelets, n (%)	*	13 (9.2)	*	*	*	17 (8.3)	*	*
Antipsychotics, n (%)	*	*	*	*	11 (8.7)	14 (6.8)	*	*
Angiotensin converting enzyme-inhibitors, n (%)	11 (18.6)	30 (21.3)	*	*	22 (17.3)	53 (25.7)	19 (18.1)	19 (18.1)
Angiotensin receptor blockers, n (%)	12 (20.3)	25 (17.7)	*	*	12 (9.4)	29 (14.1)	11 (10.5)	*
Beta-blockers, n (%)	19 (32.2)	55 (39.0)	16 (34.0)	13 (27.7)	28 (22.0)	68 (33.0)	26 (24.8)	27 (25.7)
Calcium channel blockers, n (%)	13 (22.0)	31 (22.0)	*	11 (23.4)	27 (21.3)	36 (17.5)	19 (18.1)	16 (15.2)
Diuretics, n (%)	18 (30.5)	46 (32.6)	15 (31.9)	11 (23.4)	29 (22.8)	50 (24.3)	22 (21.0)	16 (15.2)
Satins, n (%)	19 (32.2)	43 (30.5)	15 (31.9)	15 (31.9)	38 (29.9)	62 (30.1)	30 (28.6)	30 (28.6)
Antidepressants drugs, n (%)	17 (28.8)	41 (29.1)	12 (25.5)	12 (25.5)	57 (44.9)	100 (48.5)	46 (43.8)	44 (41.9)
Benzodiazepines, n (%)	12 (20.3)	42 (29.8)	11 (23.4)	11 (23.4)	15 (11.8)	28 (13.6)	13 (12.4)	12 (11.4)
Bisphosphonates, n (%)	*	29 (20.6)	*	*	26 (20.5)	22 (10.7)	15 (14.3)	15 (14.3)
CYP2D6 enzyme Inductors, n (%)	*	*	*	*	*	*	*	*
CYP2D6 enzyme Inhibitors, n (%)	*	12 (8.5)	*	*	*	11 (5.3)	*	*
Estrogens/hormone therapy, n (%)	*	12 (8.5)	*	*	*	12 (5.8)	*	*
<b>Healthcare utilization</b>								
Hospital admission, n (%)	11 (18.6)	40 (28.4)	*	*	22 (17.3)	50 (24.3)	17 (16.2)	13 (12.4)
Number of days hospitalized, mean (±SD)	*	*	*	*	*	*	*	*
Number of Medical Practitioner visits, mean (±SD)	*	*	*	*	*	*	*	*
Combined comorbidity score, mean (±SD)	*	*	*	*	*	*	*	*

<sup>†</sup> Patients with a CYP2D6-inhibiting SSRI were matched on the propensity score to at least 1 and at most 10 patients with another SSRI. A random patient in the other SSRI group was drawn from each matched set to show covariate balance resulting from the matching process.

\* Data suppressed according to CMS' current cell size suppression policy, which stipulates that no cell (e.g. admissions, discharges, patients, services) 10 or less may be displayed.

Cohort 1: Patients were exposed to tamoxifen prior to initiating an SSRI.

Cohort 2: Patients were exposed to an SSRI prior to initiating tamoxifen.



**Table G: Distribution of patient characteristics at baseline from MAX database**

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=1080	Other SSRIs n=1253	CYP2D6-inhibiting SSRIs n=911	Other SSRIs n=911 of 1225 matched	CYP2D6-inhibiting SSRIs n=1804	Other SSRIs n=1825	CYP2D6-inhibiting SSRIs n=1444	Other SSRIs n=1444 of 1669 matched
<b>Demographics</b>								
Age, mean (±SD)	50 (±9)	50 (±9)	50 (±9)	50 (±9)	50 (±9)	50 (±9)	50 (±9)	50 (±9)
Index year, n (%)								
2000	71 (6.6)	51 (4.1)	51 (5.6)	47 (5.2)	201 (11.1)	143 (7.8)	127 (8.8)	120 (8.3)
2001	229 (21.2)	183 (14.6)	171 (18.8)	157 (17.2)	334 (18.5)	273 (15.0)	242 (16.8)	240 (16.6)
2002	165 (15.3)	183 (14.6)	134 (14.7)	136 (14.9)	292 (16.2)	246 (13.5)	211 (14.6)	205 (14.2)
2003	214 (19.8)	250 (20.0)	190 (20.9)	188 (20.6)	393 (21.8)	371 (20.3)	305 (21.1)	316 (21.9)
2004	207 (19.2)	281 (22.4)	186 (20.4)	185 (20.3)	283 (15.7)	363 (19.9)	272 (18.8)	278 (19.3)
2005	102 (9.4)	138 (11.0)	89 (9.8)	94 (10.3)	148 (8.2)	210 (11.5)	138 (9.6)	144 (10.0)
2006	92 (8.5)	167 (13.3)	90 (9.9)	104 (11.4)	153 (8.5)	219 (12.0)	149 (10.3)	141 (9.8)
<b>Comorbidities</b>								
Breast cancer, n (%)	624 (57.8)	830 (66.2)	557 (61.1)	543 (59.6)	1001 (55.5)	1085 (59.5)	844 (58.4)	846 (58.6)
Breast cancer site, n (%)								
Nipple and areola	68 (6.3)	86 (6.9)	58 (6.4)	63 (6.9)	94 (5.2)	109 (6.0)	79 (5.5)	81 (5.6)
Central	141 (13.1)	186 (14.8)	121 (13.3)	125 (13.7)	188 (10.4)	218 (11.9)	166 (11.5)	155 (10.7)
Upper-inner	95 (8.8)	111 (8.9)	80 (8.8)	82 (9.0)	128 (7.1)	150 (8.2)	110 (7.6)	110 (7.6)
Lower-inner	51 (4.7)	76 (6.1)	46 (5.0)	47 (5.2)	83 (4.6)	92 (5.0)	66 (4.6)	72 (5.0)
Upper-outer	362 (33.5)	442 (35.3)	314 (34.5)	308 (33.8)	523 (29.0)	545 (29.9)	432 (29.9)	428 (29.6)
Lower-outer	78 (7.2)	88 (7.0)	58 (6.4)	66 (7.2)	115 (6.4)	125 (6.8)	98 (6.8)	89 (6.2)
Auxiliary tail	14 (1.3)	35 (2.8)	13 (1.4)	12 (1.3)	25 (1.4)	35 (1.9)	24 (1.7)	24 (1.7)
Other/Unspecified	916 (84.8)	1097 (87.5)	784 (86.1)	783 (85.9)	1386 (76.8)	1453 (79.6)	1135 (78.6)	1146 (79.4)
Breast cancer stage any time prior to SSRI, n (%)								
0	328 (30.4)	412 (32.9)	287 (31.5)	290 (31.8)	497 (27.5)	545 (29.9)	417 (28.9)	423 (29.3)
I	322 (29.8)	405 (32.3)	282 (31.0)	284 (31.2)	466 (25.8)	520 (28.5)	398 (27.6)	400 (27.7)
II	73 (6.8)	75 (6.0)	60 (6.6)	60 (6.6)	82 (4.5)	114 (6.2)	69 (4.8)	70 (4.8)
III	*	*	*	911 (100.0)	*	*	*	*
IV	*	*	*	911 (100.0)	*	*	*	*
<b>Procedures</b>								
Chemotherapy, n (%)	199 (18.4)	260 (20.8)	175 (19.2)	171 (18.8)	294 (16.3)	358 (19.6)	256 (17.7)	258 (17.9)
Mammography, n (%)	340 (31.5)	419 (33.4)	297 (32.6)	299 (32.8)	558 (30.9)	591 (32.4)	458 (31.7)	444 (30.7)
Mastectomy, n (%)	494 (45.7)	675 (53.9)	443 (48.6)	438 (48.1)	743 (41.2%)	829 (45.4%)	624 (43.2)	632 (43.8)
Radiation, n (%)	366 (33.9)	448 (35.8)	312 (34.2)	319 (35.0)	420 (23.3)	473 (25.9)	352 (24.4)	352 (24.4)
<b>Medication utilization</b>								
Pre-SSRI tamoxifen total days of supply, mean (±SD)	128 (±180)	133 (±176)	129 (±178)	133 (±181)	-	-	-	-

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=1080	Other SSRIs n=1253	CYP2D6-inhibiting SSRIs n=911	Other SSRIs n=911 of 1225 matched	CYP2D6-inhibiting SSRIs n=1804	Other SSRIs n=1825	CYP2D6-inhibiting SSRIs n=1444	Other SSRIs n=1444 of 1669 matched
Pre-tamoxifen SSRI days of supply, mean (±SD)	-	-	-	-	16 (±14)	15 (±13)	15 (±14)	16 (±13)
Number of generics, mean (±SD)	13 (±8)	14 (±9)	13 (±8)	13 (±9)	*	11 (±7)	*	*
Vaccine, n (%)	71 (6.6)	113 (9.0)	65 (7.1)	76 (8.3)	81 (4.5)	102 (5.6)	75 (5.2)	57 (3.9)
Anticoagulants, n (%)	73 (6.8)	109 (8.7)	70 (7.7)	60 (6.6)	127 (7.0)	147 (8.1)	110 (7.6)	101 (7.0)
Antiplatelets, n (%)	15 (1.4)	19 (1.5)	14 (1.5)	14 (1.5)	21 (1.2)	26 (1.4)	20 (1.4)	21 (1.5)
Antipsychotics, n (%)	137 (12.7)	178 (14.2)	125 (13.7)	130 (14.3)	305 (16.9)	362 (19.8)	264 (18.3)	267 (18.5)
Angiotensin converting enzyme-inhibitors, n (%)	178 (16.5)	203 (16.2)	144 (15.8)	157 (17.2)	308 (17.1)	272 (14.9)	233 (16.1)	221 (15.3)
Angiotensin receptor blockers, n (%)	65 (6.0)	106 (8.5)	59 (6.5)	60 (6.6)	110 (6.1)	112 (6.1)	85 (5.9)	90 (6.2)
Beta-blockers, n (%)	171 (15.8)	218 (17.4)	145 (15.9)	151 (16.6)	262 (14.5)	276 (15.1)	211 (14.6)	212 (14.7)
Calcium channel blockers, n (%)	145 (13.4)	175 (14.0)	117 (12.8)	118 (13.0)	271 (15.0)	220 (12.1)	190 (13.2)	188 (13.0)
Diuretics, n (%)	205 (19.0)	226 (18.0)	161 (17.7)	172 (18.9)	341 (18.9)	328 (18.0)	264 (18.3)	262 (18.1)
Satins, n (%)	149 (13.8)	209 (16.7)	131 (14.4)	135 (14.8)	287 (15.9)	295 (16.2)	227 (15.7)	229 (15.9)
Antidepressants drugs, n (%)	595 (55.1)	684 (54.6)	491 (53.9)	483 (53.0)	531 (29.4)	571 (31.3)	438 (30.3)	421 (29.2)
Benzodiazepines, n (%)	490 (45.4)	584 (46.6)	409 (44.9)	417 (45.8)	755 (41.9)	786 (43.1)	606 (42.0)	597 (41.3)
Bisphosphonates, n (%)	52 (4.8)	50 (4.0)	38 (4.2)	41 (4.5)	62 (3.4)	52 (2.8)	46 (3.2)	47 (3.3)
CYP2D6 enzyme Inductors, n (%)	178 (16.5)	228 (18.2)	160 (17.6)	153 (16.8)	237 (13.1)	286 (15.7)	210 (14.5)	215 (14.9)
CYP2D6 enzyme Inhibitors, n (%)	479 (44.4)	436 (34.8)	365 (40.1)	365 (40.1)	256 (14.2)	303 (16.6)	220 (15.2)	218 (15.1)
Estrogens/hormone therapy, n (%)	134 (12.4)	139 (11.1)	102 (11.2)	105 (11.5)	213 (11.8)	185 (10.1)	154 (10.7)	154 (10.7)
<b>Healthcare utilization</b>								
Hospital admission, n (%)	344 (31.9)	426 (34.0)	301 (33.0)	298 (32.7)	451 (25.0)	474 (26.0)	370 (25.6)	381 (26.4)
Number of days hospitalized, mean (±SD)	*	*	*	*	*	*	*	*
Number of Medical Practitioner visits, mean (±SD)	12 (±12)	12 (±12)	12 (±12)	12 (±12)	*	*	*	*
Combined comorbidity score, mean (±SD)	*	*	*	*	*	*	*	*

<sup>†</sup> Patients with a CYP2D6-inhibiting SSRI were matched on the propensity score to at least 1 and at most 10 patients with another SSRI. A random patient in the other SSRI group was drawn from each matched set to show covariate balance resulting from the matching process.

\* Data suppressed according to CMS' current cell size suppression policy, which stipulates that no cell (e.g. admissions, discharges, patients, services) 10 or less may be displayed.

Cohort 1: Patients were exposed to tamoxifen prior to initiating an SSRI.

Cohort 2: Patients were exposed to an SSRI prior to initiating tamoxifen.

**Table H: Distribution of patient characteristics at baseline from PAAD database**

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=117	Other SSRIs n=125	CYP2D6-inhibiting SSRIs n=79	Other SSRIs n=79 of 122 matched	CYP2D6-inhibiting SSRIs n=135	Other SSRIs n=136	CYP2D6-inhibiting SSRIs n=93	Other SSRIs n=93 of 133 matched
<b>Demographics</b>								
Age, mean (±SD)	77 (±10)	78 (±8)	77 (±10)	78 (±8)	75 (±11)	75 (±10)	76 (±11)	75 (±11)
Index year, n (%)								
1995	*	*	*	*	*	*	*	*
1996	*	*	*	*	12 (8.9)	15 (11.0)	*	*
1997	14 (12.0)	*	*	*	11 (8.1)	*	*	*
1998	12 (10.3)	*	*	*	*	13 (9.6)	*	*
1999	11 (9.4)	*	*	*	13 (9.6)	*	*	*
2000	16 (13.7)	22 (17.6)	14 (17.7)	14 (17.7)	18 (13.3)	15 (11.0)	12 (12.9)	13 (14.0)
2001	15 (12.8)	13 (10.4)	*	11 (13.9)	21 (15.6)	17 (12.5)	12 (12.9)	*
2002	14 (12.0)	21 (16.8)	11 (13.9)	*	12 (8.9)	15 (11.0)	*	14 (15.1)
2003	*	15 (12.0)	*	*	12 (8.9)	15 (11.0)	*	*
2004	*	*	*	*	12 (8.9)	16 (11.8)	*	*
2005	*	*	*	*	*	*	*	*
<b>Comorbidities</b>								
Breast cancer, n (%)	84 (71.8)	78 (62.4)	54 (68.4)	51 (64.6)	74 (54.8)	79 (58.1)	55 (59.1)	53 (57.0)
Breast cancer site, n (%)								
Nipple and areola								
Central	12 (10.3)	12 (9.6)	*	*	13 (9.6)	*	*	*
Upper-inner	17 (14.5)	19 (15.2)	13 (16.5)	*	16 (11.9)	12 (8.8)	*	*
Lower-inner	*	11 (8.8)	*	*	*	*	*	*
Upper-outer	12 (10.3)	*	*	*	*	*	*	*
Lower-outer	41 (35.0)	46 (36.8)	25 (31.6)	24 (30.4)	29 (21.5)	33 (24.3)	22 (23.7)	24 (25.8)
Auxiliary tail	*	15 (12.0)	*	*	*	13 (9.6)	*	*
Other/Unspecified	*	*	*	*	*	*	*	*
Other/Unspecified	104 (88.9)	110 (88.0)	69 (87.3)	69 (87.3)	96 (71.1)	100 (73.5)	69 (74.2)	68 (73.1)
Breast cancer stage any time prior to SSRI, n (%)								
0	36 (30.8)	55 (44.0)	28 (35.4)	28 (35.4)	34 (25.2)	37 (27.2)	26 (28.0)	23 (24.7)
I	36 (30.8)	53 (42.4)	28 (35.4)	28 (35.4)	33 (24.4)	33 (24.3)	25 (26.9)	22 (23.7)
II	*	*	*	*	*	*	*	*
III	*	*	*	79 (100.0)	*	*	*	*
IV	*	125 (100.0)	*	79 (100.0)	*	*	*	*
<b>Procedures</b>								
Chemotherapy, n (%)	*	*	*	*	22 (16.3)	*	*	*
Mammography, n (%)	45 (38.5)	47 (37.6)	26 (32.9)	34 (43.0)	42 (31.1)	45 (33.1)	30 (32.3)	28 (30.1)
Mastectomy, n (%)	81 (69.2)	85 (68.0)	56 (70.9)	54 (68.4)	53 (39.3)	60 (44.1)	40 (43.0)	39 (41.9)
Radiation, n (%)	37 (31.6)	33 (26.4)	23 (29.1)	22 (27.8)	20 (14.8)	16 (11.8)	11 (11.8)	13 (14.0)
<b>Medication utilization</b>								

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=117	Other SSRIs n=125	CYP2D6-inhibiting SSRIs n=79	Other SSRIs n=79 of 122 matched	CYP2D6-inhibiting SSRIs n=135	Other SSRIs n=136	CYP2D6-inhibiting SSRIs n=93	Other SSRIs n=93 of 133 matched
Pre-SSRI tamoxifen total days of supply, mean (±SD)	319 (±359)	396 (±489)	354 (±385)	370 (±468)	-	-	-	-
Pre-tamoxifen SSRI days of supply, mean (±SD)	-	-	-	-	32 (±84)	23 (±44)	21 (±22)	28 (±52)
Number of generics, mean (±SD)	15 (±8)	15 (±10)	15 (±9)	14 (±9)	*	*	*	*
Vaccine, n (%)	33 (28.2)	37 (29.6)	22 (27.8)	23 (29.1)	11 (8.1)	18 (13.2)	11 (11.8)	*
Anticoagulants, n (%)	14 (12.0)	16 (12.8)	*	*	12 (8.9)	*	*	*
Antiplatelets, n (%)	*	*	*	*	*	*	*	*
Antipsychotics, n (%)	*	*	*	*	*	14 (10.3)	*	11 (11.8)
Angiotensin converting enzyme-inhibitors, n (%)	30 (25.6)	37 (29.6)	20 (25.3)	19 (24.1)	29 (21.5)	29 (21.3)	22 (23.7)	22 (23.7)
Angiotensin receptor blockers, n (%)	17 (14.5)	22 (17.6)	12 (15.2)	*	22 (16.3)	18 (13.2)	12 (12.9)	11 (11.8)
Beta-blockers, n (%)	48 (41.0)	47 (37.6)	31 (39.2)	27 (34.2)	35 (25.9)	39 (28.7)	24 (25.8)	27 (29.0)
Calcium channel blockers, n (%)	45 (38.5)	55 (44.0)	32 (40.5)	34 (43.0)	47 (34.8)	46 (33.8)	33 (35.5)	33 (35.5)
Diuretics, n (%)	50 (42.7)	52 (41.6)	36 (45.6)	33 (41.8)	32 (23.7)	33 (24.3)	21 (22.6)	21 (22.6)
Satins, n (%)	26 (22.2)	30 (24.0)	16 (20.3)	19 (24.1)	22 (16.3)	32 (23.5)	20 (21.5)	19 (20.4)
Antidepressants drugs, n (%)	41 (35.0)	41 (32.8)	25 (31.6)	31 (39.2)	11 (8.1)	14 (10.3)	*	*
Benzodiazepines, n (%)	69 (59.0)	52 (41.6)	44 (55.7)	42 (53.2)	53 (39.3)	54 (39.7)	37 (39.8)	35 (37.6)
Bisphosphonates, n (%)	*	*	*	*	*	12 (8.8)	*	*
CYP2D6 enzyme Inductors, n (%)	*	*	*	*	*	*	*	*
CYP2D6 enzyme Inhibitors, n (%)	31 (26.5)	30 (24.0)	18 (22.8)	21 (26.6)	*	*	*	*
Estrogens/hormone therapy, n (%)	19 (16.2)	17 (13.6)	*	13 (16.5)	12 (8.9)	*	*	*
<b>Healthcare utilization</b>								
Hospital admission, n (%)	71 (60.7)	69 (55.2)	46 (58.2)	44 (55.7)	53 (39.3)	58 (42.6)	39 (41.9)	37 (39.8)
Number of days hospitalized, mean (±SD)	*	*	*	*	*	*	*	*
Number of Medical Practitioner visits, mean (±SD)	19 (±20)	22 (±29)	20 (±23)	20 (±23)	*	*	*	*
Combined comorbidity score, mean (±SD)	*	*	*	*	*	*	*	*

<sup>†</sup> Patients with a CYP2D6-inhibiting SSRI were matched on the propensity score to at least 1 and at most 10 patients with another SSRI. A random patient in the other SSRI group was drawn from each matched set to show covariate balance resulting from the matching process.

\* Data suppressed according to CMS' current cell size suppression policy, which stipulates that no cell (e.g. admissions, discharges, patients, services) 10 or less may be displayed.

Cohort 1: Patients were exposed to tamoxifen prior to initiating an SSRI.

Cohort 2: Patients were exposed to an SSRI prior to initiating tamoxifen.

**Table I: Distribution of patient characteristics at baseline from PACE database**

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=267	Other SSRIs n=381	CYP2D6-inhibiting SSRIs n=249	Other SSRIs n=249 of 375 matched	CYP2D6-inhibiting SSRIs n=241	Other SSRIs n=238	CYP2D6-inhibiting SSRIs n=174	Other SSRIs n=174 of 236 matched
<b>Demographics</b>								
Age, mean (±SD)	79 (±7)	79 (±6)	79 (±7)	79 (±6)	78 (±7)	79 (±7)	78 (±7)	79 (±7)
Index year, n (%)								
1995	78 (29.2)	109 (28.6)	75 (30.1)	71 (28.5)	71 (29.5)	64 (26.9)	53 (30.5)	50 (28.7)
1996	36 (13.5)	52 (13.6)	34 (13.7)	33 (13.3)	16 (6.6)	18 (7.6)	13 (7.5)	13 (7.5)
1997	29 (10.9)	35 (9.2)	26 (10.4)	28 (11.2)	19 (7.9)	23 (9.7)	13 (7.5)	15 (8.6)
1998	33 (12.4)	28 (7.3)	27 (10.8)	25 (10.0)	28 (11.6)	11 (4.6)	12 (6.9)	11 (6.3)
1999	24 (9.0)	30 (7.9)	22 (8.8)	26 (10.4)	20 (8.3)	22 (9.2)	17 (9.8)	15 (8.6)
2000	17 (6.4)	26 (6.8)	16 (6.4)	12 (4.8)	21 (8.7)	12 (5.0)	14 (8.0)	12 (6.9)
2001	21 (7.9)	35 (9.2)	21 (8.4)	22 (8.8)	19 (7.9)	25 (10.5)	15 (8.6)	16 (9.2)
2002	16 (6.0)	23 (6.0)	15 (6.0)	17 (6.8)	17 (7.1)	17 (7.1)	12 (6.9)	16 (9.2)
2003	*	17 (4.5)	*	*	13 (5.4)	19 (8.0)	12 (6.9)	15 (8.6)
2004	*	*	*	*	*	14 (5.9)	*	*
2005	*	18 (4.7)	*	*	*	13 (5.5)	*	*
<b>Comorbidities</b>								
Breast cancer, n (%)	133 (49.8)	180 (47.2)	119 (47.8)	122 (49.0)	108 (44.8)	101 (42.4)	79 (45.4)	75 (43.1)
Breast cancer site, n (%)								
Nipple and areola	25 (9.4)	29 (7.6)	19 (7.6)	21 (8.4)	11 (4.6)	13 (5.5)	*	*
Central	35 (13.1)	58 (15.2)	35 (14.1)	37 (14.9)	27 (11.2)	26 (10.9)	20 (11.5)	18 (10.3)
Upper-inner	13 (4.9)	21 (5.5)	13 (5.2)	14 (5.6)	17 (7.1)	18 (7.6)	12 (6.9)	11 (6.3)
Lower-inner	18 (6.7)	21 (5.5)	13 (5.2)	16 (6.4)	*	*	*	*
Upper-outer	88 (33.0)	112 (29.4)	79 (31.7)	78 (31.3)	51 (21.2)	60 (25.2)	38 (21.8)	36 (20.7)
Lower-outer	19 (7.1)	26 (6.8)	18 (7.2)	17 (6.8)	13 (5.4)	*	*	*
Auxiliary tail	*	*	*	*	*	*	*	*
Other/Unspecified	238 (89.1)	330 (86.6)	220 (88.4)	216 (86.7)	184 (76.3)	176 (73.9)	134 (77.0)	130 (74.7)
Breast cancer stage any time prior to SSRI, n (%)								
0	55 (20.6)	91 (23.9)	52 (20.9)	56 (22.5)	42 (17.4)	42 (17.6)	30 (17.2)	27 (15.5)
I	54 (20.2)	90 (23.6)	51 (20.5)	55 (22.1)	42 (17.4)	40 (16.8)	30 (17.2)	27 (15.5)
II	11 (4.1)	24 (6.3)	11 (4.4)	14 (5.6)	*	*	*	*
III	*	*	*	249 (100.0)	*	*	*	*
IV	*	*	*	249 (100.0)	*	*	*	*
<b>Procedures</b>								
Chemotherapy, n (%)	*	13 (3.4)	*	11 (4.4)	13 (5.4)	*	*	*
Mammography, n (%)	67 (25.1)	106 (27.8)	64 (25.7)	66 (26.5)	73 (30.3)	63 (26.5)	50 (28.7)	49 (28.2)
Mastectomy, n (%)	116 (43.4)	169 (44.4)	104 (41.8)	110 (44.2)	80 (33.2)	82 (34.5)	53 (30.5)	55 (31.6)
Radiation, n (%)	63 (23.6)	95 (24.9)	61 (24.5)	60 (24.1)	26 (10.8)	31 (13.0)	19 (10.9)	19 (10.9)
<b>Medication utilization</b>								

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=267	Other SSRIs n=381	CYP2D6-inhibiting SSRIs n=249	Other SSRIs n= 249 of 375 matched	CYP2D6-inhibiting SSRIs n=241	Other SSRIs n=238	CYP2D6-inhibiting SSRIs n=174	Other SSRIs n=174 of 236 matched
Pre-SSRI tamoxifen total days of supply, mean (±SD)	287 (±353)	311 (±400)	279 (±342)	287 (±343)	-	-	-	-
Pre-tamoxifen SSRI days of supply, mean (±SD)	-	-	-	-	13 (±10)	13 (±10)	13 (±10)	12 (±10)
Number of generics, mean (±SD)	12 (±6)	12 (±7)	12 (±6)	12 (±6)	*	*	*	*
Vaccine, n (%)	45 (16.9)	75 (19.7)	42 (16.9)	43 (17.3)	24 (10.0)	22 (9.2)	16 (9.2)	19 (10.9)
Anticoagulants, n (%)	28 (10.5)	53 (13.9)	27 (10.8)	25 (10.0)	24 (10.0)	33 (13.9)	21 (12.1)	17 (9.8)
Antiplatelets, n (%)	11 (4.1)	17 (4.5)	11 (4.4)	*	*	*	*	*
Antipsychotics, n (%)	23 (8.6)	28 (7.3)	21 (8.4)	24 (9.6)	12 (5.0)	22 (9.2)	11 (6.3)	14 (8.0)
Angiotensin converting enzyme-inhibitors, n (%)	68 (25.5)	112 (29.4)	67 (26.9)	69 (27.7)	67 (27.8)	62 (26.1)	47 (27.0)	48 (27.6)
Angiotensin receptor blockers, n (%)	15 (5.6)	36 (9.4)	15 (6.0)	17 (6.8)	*	17 (7.1)	*	*
Beta-blockers, n (%)	83 (31.1)	122 (32.0)	80 (32.1)	74 (29.7)	60 (24.9)	67 (28.2)	50 (28.7)	47 (27.0)
Calcium channel blockers, n (%)	97 (36.3)	159 (41.7)	95 (38.2)	91 (36.5)	86 (35.7)	77 (32.4)	59 (33.9)	60 (34.5)
Diuretics, n (%)	51 (19.1)	107 (28.1)	49 (19.7)	45 (18.1)	60 (24.9)	61 (25.6)	45 (25.9)	43 (24.7)
Satins, n (%)	31 (11.6)	64 (16.8)	31 (12.4)	28 (11.2)	31 (12.9)	40 (16.8)	24 (13.8)	23 (13.2)
Antidepressants drugs, n (%)	99 (37.1)	130 (34.1)	89 (35.7)	82 (32.9)	28 (11.6)	21 (8.8)	18 (10.3)	20 (11.5)
Benzodiazepines, n (%)	138 (51.7)	160 (42.0)	125 (50.2)	124 (49.8)	98 (40.7)	80 (33.6)	67 (38.5)	64 (36.8)
Bisphosphonates, n (%)	21 (7.9)	40 (10.5)	21 (8.4)	21 (8.4)	11 (4.6)	*	*	*
CYP2D6 enzyme Inductors, n (%)	*	*	*	*	*	*	*	*
CYP2D6 enzyme Inhibitors, n (%)	83 (31.1)	102 (26.8)	74 (29.7)	73 (29.3)	18 (7.5)	13 (5.5)	11 (6.3)	12 (6.9)
Estrogens/hormone therapy, n (%)	32 (12.0)	40 (10.5)	30 (12.0)	26 (10.4)	22 (9.1)	25 (10.5)	16 (9.2)	13 (7.5)
<b>Healthcare utilization</b>								
Hospital admission, n (%)	144 (53.9)	223 (58.5)	136 (54.6)	135 (54.2)	96 (39.8)	109 (45.8)	76 (43.7)	74 (42.5)
Number of days hospitalized, mean (±SD)	*	*	*	*	*	*	*	*
Number of Medical Practitioner visits, mean (±SD)	15 (±15)	16 (±16)	15 (±15)	15 (±15)	*	*	*	*
Combined comorbidity score, mean (±SD)	*	*	*	*	*	*	*	*

<sup>†</sup> Patients with a CYP2D6-inhibiting SSRI were matched on the propensity score to at least 1 and at most 10 patients with another SSRI. A random patient in the other SSRI group was drawn from each matched set to show covariate balance resulting from the matching process.

\* Data suppressed according to CMS' current cell size suppression policy, which stipulates that no cell (e.g. admissions, discharges, patients, services) 10 or less may be displayed.

Cohort 1: Patients were exposed to tamoxifen prior to initiating an SSRI.

Cohort 2: Patients were exposed to an SSRI prior to initiating tamoxifen.

**Table J: Distribution of patient characteristics at baseline from Optum Research database**

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=745	Other SSRIs n=1899	CYP2D6-inhibiting SSRIs n=740	Other SSRIs n=740 of 1898	CYP2D6-inhibiting SSRIs n=1224	Other SSRIs n=2529	CYP2D6-inhibiting SSRIs n=1209	Other SSRIs n=1209 of 2528 matched
<b>Demographics</b>								
Age, mean (±SD)	54 (±10)	51 (±10)	54 (±10)	53 (±10)	53 (±10)	51 (±10)	53 (±10)	52 (±10)
Index year, n (%)								
2004	390 (52.3)	579 (30.5)	387 (52.3)	379 (51.2)	584 (47.7)	665 (26.3)	564 (46.7)	563 (46.6)
2005	62 (8.3)	156 (8.2)	60 (8.1)	63 (8.5)	103 (8.4)	183 (7.2)	102 (8.4)	96 (7.9)
2006	51 (6.8)	144 (7.6)	51 (6.9)	47 (6.4)	82 (6.7)	196 (7.8)	84 (6.9)	93 (7.7)
2007	53 (7.1)	150 (7.9)	53 (7.2)	54 (7.3)	75 (6.1)	209 (8.3)	78 (6.5)	83 (6.9)
2008	43 (5.8)	161 (8.5)	43 (5.8)	53 (7.2)	88 (7.2)	228 (9.0)	88 (7.3)	80 (6.6)
2009	34 (4.6)	143 (7.5)	34 (4.6)	34 (4.6)	64 (5.2)	242 (9.6)	62 (5.1)	60 (5.0)
2010	25 (3.4)	129 (6.8)	25 (3.4)	23 (3.1)	50 (4.1)	190 (7.5)	50 (4.1)	63 (5.2)
2011	32 (4.3)	142 (7.5)	32 (4.3)	37 (5.0)	57 (4.7)	209 (8.3)	57 (4.7)	44 (3.6)
2012	27 (3.6)	151 (8.0)	27 (3.6)	23 (3.1)	67 (5.5)	201 (7.9)	66 (5.5)	73 (6.0)
2013	28 (3.8)	144 (7.6)	28 (3.8)	27 (3.6)	54 (4.4)	206 (8.1)	58 (4.8)	54 (4.5)
<b>Comorbidities</b>								
Breast cancer, n (%)	294 (39.5)	1044 (55.0)	293 (39.6)	301 (40.7)	562 (45.9)	1392 (55.0)	555 (45.9)	572 (47.3)
Breast cancer site, n (%)								
Nipple and areola	31 (4.2)	96 (5.1)	31 (4.2)	32 (4.3)	45 (3.7)	92 (3.6)	44 (3.6)	40 (3.3)
Central	53 (7.1)	238 (12.5)	53 (7.2)	63 (8.5)	90 (7.4)	269 (10.6)	89 (7.4)	90 (7.4)
Upper-inner	50 (6.7)	226 (11.9)	50 (6.8)	50 (6.8)	70 (5.7)	255 (10.1)	70 (5.8)	74 (6.1)
Lower-inner	35 (4.7)	109 (5.7)	35 (4.7)	34 (4.6)	54 (4.4)	137 (5.4)	54 (4.5)	58 (4.8)
Upper-outer	195 (26.2)	703 (37.0)	195 (26.4)	205 (27.7)	297 (24.3)	831 (32.9)	296 (24.5)	306 (25.3)
Lower-outer	42 (5.6)	175 (9.2)	42 (5.7)	40 (5.4)	62 (5.1)	206 (8.1)	62 (5.1)	67 (5.5)
Auxiliary tail	5 (0.7)	25 (1.3)	5 (0.7)	6 (0.8)	18 (1.5)	32 (1.3)	16 (1.3)	17 (1.4)
Other/Unspecified	484 (65.0)	1500 (79.0)	482 (65.1)	486 (65.7)	677 (55.3)	1741 (68.8)	670 (55.4)	690 (57.1)
Breast cancer stage any time prior to SSRI, n (%)								
0	206 (27.7)	782 (41.2)	204 (27.6)	224 (30.3)	341 (27.9)	914 (36.1)	337 (27.9)	345 (28.5)
I	195 (26.2)	757 (39.9)	193 (26.1)	215 (29.1)	320 (26.1)	865 (34.2)	316 (26.1)	327 (27.0)
II	30 (4.0)	144 (7.6)	30 (4.1)	33 (4.5)	59 (4.8)	191 (7.6)	58 (4.8)	53 (4.4)
III	1 (0.1)	4 (0.2)	1 (0.1)	1 (0.1)	2 (0.2)	3 (0.1)	2 (0.2)	1 (0.1)
IV	1 (0.1)	3 (0.2)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.1)	1 (0.1)	0 (0)
<b>Procedures</b>								
Chemotherapy, n (%)	102 (13.7)	388 (20.4)	102 (13.8)	105 (14.2)	188 (15.4)	514 (20.3)	185 (15.3)	191 (15.8)
Mammography, n (%)	311 (41.7)	1083 (57.0)	308 (41.6)	319 (43.1)	534 (43.6)	1481 (58.6)	532 (44.0)	539 (44.6)
Mastectomy, n (%)	230 (30.9)	968 (51.0)	230 (31.1)	234 (31.6)	248 (20.3)	820 (32.4)	411 (34.0)	418 (34.6)
Radiation, n (%)	184 (24.7)	671 (35.3)	182 (24.6)	189 (25.5)	242 (19.8)	686 (27.1)	241 (19.9)	255 (21.1)
<b>Medication utilization</b>								

	Cohort 1				Cohort 2			
	Unmatched		Matched (1:10) <sup>†</sup>		Unmatched		Matched (1:10) <sup>†</sup>	
	CYP2D6-inhibiting SSRIs n=745	Other SSRIs n=1899	CYP2D6-inhibiting SSRIs n=740	Other SSRIs n=740 of 1898	CYP2D6-inhibiting SSRIs n=1224	Other SSRIs n=2529	CYP2D6-inhibiting SSRIs n=1209	Other SSRIs n=1209 of 2528 matched
Pre-SSRI tamoxifen total days of supply, mean (±SD)	113 (±149)	151 (±204)	113 (±149)	111 (±139)	-	-	-	-
Pre-tamoxifen SSRI days of supply, mean (±SD)	-	-	-	-	17 (±18)	19 (±20)	17 (±18)	17 (±20)
Number of generics, mean (±SD)	8 (±6)	9 (±6)	8 (±6)	8 (±6)	5 (±5)	7 (±5)	5 (±5)	5 (±5)
Vaccine, n (%)	75 (10.1)	240 (12.6)	75 (10.1)	81 (10.9)	80 (6.5)	209 (8.3)	79 (6.5)	80 (6.6)
Anticoagulants, n (%)	35 (4.7)	94 (4.9)	35 (4.7)	30 (4.1)	38 (3.1)	103 (4.1)	38 (3.1)	34 (2.8)
Antiplatelets, n (%)	6 (0.8)	19 (1.0)	6 (0.8)	4 (0.5)	8 (0.7)	19 (0.8)	8 (0.7)	7 (0.6)
Antipsychotics, n (%)	17 (2.3)	54 (2.8)	16 (2.2)	17 (2.3)	25 (2.0)	60 (2.4)	25 (2.1)	24 (2.0)
Angiotensin converting enzyme-inhibitors, n (%)	95 (12.8)	162 (8.5)	92 (12.4)	89 (12.0)	125 (10.2)	214 (8.5)	118 (9.8)	127 (10.5)
Angiotensin receptor blockers, n (%)	62 (8.3)	137 (7.2)	61 (8.2)	67 (9.1)	71 (5.8)	156 (6.2)	71 (5.9)	74 (6.1)
Beta-blockers, n (%)	98 (13.2)	198 (10.4)	96 (13.0)	78 (10.5)	154 (12.6)	260 (10.3)	144 (11.9)	145 (12.0)
Calcium channel blockers, n (%)	57 (7.7)	128 (6.7)	57 (7.7)	50 (6.8)	66 (5.4)	141 (5.6)	66 (5.5)	65 (5.4)
Diuretics, n (%)	80 (10.7)	185 (9.7)	78 (10.5)	73 (9.9)	104 (8.5)	193 (7.6)	96 (7.9)	91 (7.5)
Satins, n (%)	106 (14.2)	241 (12.7)	105 (14.2)	93 (12.6)	166 (13.6)	333 (13.2)	159 (13.2)	168 (13.9)
Antidepressants drugs, n (%)	282 (37.9)	787 (41.4)	278 (37.6)	268 (36.2)	171 (14.0)	362 (14.3)	168 (13.9)	173 (14.3)
Benzodiazepines, n (%)	233 (31.3)	817 (43.0)	233 (31.5)	232 (31.4)	354 (28.9)	902 (35.7)	352 (29.1)	371 (30.7)
Bisphosphonates, n (%)	38 (5.1)	131 (6.9)	38 (5.1)	36 (4.9)	59 (4.8)	104 (4.1)	58 (4.8)	59 (4.9)
CYP2D6 enzyme Inductors, n (%)	74 (9.9)	288 (15.2)	74 (10.0)	75 (10.1)	132 (10.8)	390 (15.4)	129 (10.7)	134 (11.1)
CYP2D6 enzyme Inhibitors, n (%)	218 (29.3)	435 (22.9)	214 (28.9)	210 (28.4)	110 (9.0)	338 (13.4)	110 (9.1)	127 (10.5)
Estrogens/hormone therapy, n (%)	71 (9.5)	182 (9.6)	69 (9.3)	67 (9.1)	85 (6.9)	231 (9.1)	85 (7.0)	83 (6.9)
<b>Healthcare utilization</b>								
Hospital admission, n (%)	118 (15.8)	400 (21.1)	117 (15.8)	117 (15.8)	133 (10.9)	392 (15.5)	133 (11.0)	125 (10.3)
Number of days hospitalized, mean (±SD)	1 (±3)	1 (±5)	1 (±3)	1 (±5)	1 (±2)	1 (±5)	1 (±2)	0 (±2)
Number of Medical Practitioner visits, mean (±SD)	8 (±10)	12 (±11)	8 (±10)	9 (±9)	5 (±6)	7 (±6)	5 (±6)	5 (±6)
Combined comorbidity score, mean (±SD)	2 (±2)	2 (±2)	2 (±2)	1 (±2)	1 (±2)	2 (±2)	1 (±2)	1 (±2)

<sup>†</sup> Patients with a CYP2D6-inhibiting SSRI were matched on the propensity score to at least 1 and at most 10 patients with another SSRI. A random patient in the other SSRI group was drawn from each matched set to show covariate balance resulting from the matching process.

\* Data suppressed according to CMS' current cell size suppression policy, which stipulates that no cell (e.g. admissions, discharges, patients, services) 10 or less may be displayed.

Cohort 1: Patients were exposed to tamoxifen prior to initiating an SSRI.

Cohort 2: Patients were exposed to an SSRI prior to initiating tamoxifen