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## **Endocrine therapy use among elderly hormone receptor-positive breast cancer patients enrolled in Medicare Part D**

*Gerald F. Riley<sup>1</sup>, Joan L. Warren<sup>2</sup>, Linda C. Harlan<sup>2</sup>, and Steven A. Blackwell<sup>1</sup>*

<sup>1</sup>U.S. Department of Health and Human Services, Centers for Medicare & Medicaid Services

<sup>2</sup> National Cancer Institute, Applied Research Program

### **Abstract**

**Background:** Clinical guidelines recommend that women with hormone-receptor positive breast cancer receive endocrine therapy (selective estrogen receptor modulators [SERMs] or aromatase inhibitors [AIs]) for five years following diagnosis.

**Objective:** To examine utilization and adherence to therapy for SERMs and AIs in Medicare Part D prescription drug plans.

**Data:** Linked Surveillance, Epidemiology, and End Results (SEER)-Medicare data.

**Study design:** We identified 15,542 elderly women diagnosed with hormone-receptor positive breast cancer in years 2003–2005 (the latest SEER data at the time of the study) and enrolled in a Part D plan in 2006 or 2007 (the initial years of Part D). This permitted us to compare utilization and adherence to therapy at various points within the recommended five-year timeframe for endocrine therapy. SERM and AI use was measured from claim records. Non-adherence to therapy was defined as a medication possession ratio of less than 80 percent.

**Principal findings:** Between May 2006 and December 2007, 22 percent of beneficiaries received SERM, 52 percent AI, and 26 percent received neither. The percent receiving any endocrine therapy decreased with time from diagnosis. Among SERM and AI users, 20–30 percent were non-adherent to therapy; out-of-pocket costs were higher for AI than SERM and were strongly associated with non-adherence. For AI users without a low income subsidy, adherence to therapy deteriorated after reaching the Part D coverage gap.

**Conclusions:** Many elderly breast cancer patients were not receiving therapy for the recommended five years following diagnosis. Choosing a Part D plan that minimizes out-of-pocket costs is critical to ensuring beneficiary access to essential medications.

**Keywords:** Breast cancer, endocrine therapy, adherence, Part D

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## Introduction

Since January 2006, Medicare beneficiaries have had access to prescription drug benefits under the Part D program through enrollment in a Medicare Advantage prescription drug plan (MAPD) or a stand-alone drug plan (PDP). Under both plan types, the standard Part D benefit package includes an annual deductible (\$250 in 2006) after which a 25-percent coinsurance rate applies up to an initial coverage limit (\$2,250 in 2006). After reaching the initial coverage limit, the enrollee enters a coverage gap (or “donut hole”) during which he or she is responsible for 100 percent of all drug costs. If the enrollee reaches an out-of-pocket threshold (\$3,600 in 2006), catastrophic coverage begins with a five-percent coinsurance rate (Hoadley, 2006). As an alternative to the standard Part D benefit, plans may elect to offer actuarially equivalent coverage or enhanced benefits with more comprehensive drug coverage. Some Part D plans with enhanced benefits provide them in the coverage gap, and they are often limited to generic drugs and sometimes also cover selected brand name drugs. Many plans offer different levels of coverage (referred to as tiers) within their formulary of covered drugs, with lower amounts of cost sharing usually associated with generics and preferred brand name drugs (Hoadley, Hargrave, Cubanski, & Newman, 2006).

Part D plans typically charge a monthly premium, which averaged \$37 in PDPs and \$18 in MAPDs in 2006 (Gold, 2006). Beneficiaries with income and assets below specified levels, including those who are dually eligible for Medicare and Medicaid, may qualify to receive a low income subsidy (LIS), covering all or part of the Part D premium and most enrollee cost sharing, as well as costs in the coverage gap. Enrollment in Part D plans is voluntary; beneficiaries may continue to receive drug coverage from other sources in lieu of enrolling in a Part D plan or may choose to go without drug coverage. Dual eligibles are assigned to a PDP if they do not enroll in a plan voluntarily. As of January 2011, 28.4 million Medicare beneficiaries were enrolled in Part D plans (Centers for Medicare & Medicaid Services, 2011).

There is substantial variation in the benefits offered by Part D plans; the variation in out-of-pocket costs may influence beneficiary receipt of drug therapy (Goldman, Joyce, & Zheng, 2007; Maciejewski, Farley, Parker, & Wansink, 2010; Choudhry et al., 2010). For non-LIS enrollees, cost-sharing prior to the coverage gap may include deductibles, fixed dollar copayments, coinsurance rates (i.e., a percentage of total costs), and classification of covered drugs into tiers with different levels of cost sharing. Most plans do not offer benefits in the coverage gap, although some offer coverage for lower tier drugs. Cost-sharing also varies for LIS enrollees, primarily related to income level and use of brand name vs. generic drugs.

Under Part D, Medicare covers adjuvant endocrine therapy, which has been shown to improve survival among women treated for breast cancer (Early Breast Cancer Trialists' Collaborative Group, 2005; The ATAC Trialists' Group, 2002; Breast International Group [BIG] I-98 Collaborative Group, 2005). Two classes of endocrine therapy medications are covered:

selective estrogen receptor modulators (SERMs)—of which tamoxifen is the most commonly prescribed—and aromatase inhibitors (AIs). Tamoxifen has been widely prescribed since the 1970s and is available in generic form. Its use increased among breast cancer patients in the 1980s and 1990s (Harlan et al., 2006). The first AIs were approved for use in the 1990s and are available as brand name drugs only. AI use has increased rapidly (Svahn et al., 2009; Aiello et al., 2008) and is displacing tamoxifen as the first course of endocrine therapy, following clinical trials that reported greater efficacy for AIs compared to tamoxifen (The ATAC Trialists' Group, 2002; BIG I-98 Collaborative Group, 2005). The National Comprehensive Cancer Network guidelines currently call for either SERMs or AIs to be provided to postmenopausal women with hormone receptor-positive breast cancer for a five year period following diagnosis (National Comprehensive Cancer Network, 2011). To achieve the maximum benefit, patients must receive endocrine therapy for the full five years (Early Breast Cancer Trialists' Collaborative Group, 2005).

Part D records indicate the total cost per month for AIs was \$243 compared to \$31 for SERMs in years 2006–2007, reflecting the availability of SERMs, but not AIs, in generic form. Out-of-pocket costs differed as well, averaging \$70.15 for AIs and \$8.19 for SERMs, for enrollees without LIS. Among AI users without LIS or benefits in the coverage gap, 71 percent reached the coverage gap in either 2006 or 2007 (data not in tables). Among SERM users, only 20 percent did so.

The purpose of this study was to examine patterns of utilization and adherence to therapy, for SERM and AI, among elderly women diagnosed with hormone-receptor positive breast cancer and enrolled in a Medicare Part D prescription drug plan. Most previous studies have examined use of adjuvant endocrine therapy among elderly breast cancer patients prior to the introduction of Part D drug coverage, and many have been limited to smaller samples of patients or to specific health plans and providers (Svahn et al., 2009; Aiello et al., 2008; Lash, Fox, Westrup, Fink, & Silliman, 2006; Owusu et al., 2008; Hershman et al., 2010; Partridge, Wang, Winer, & Avorn, 2003). This analysis adds to the literature by examining utilization patterns subsequent to the introduction of Part D coverage among a large and diverse sample of elderly breast cancer patients treated in a variety of clinical settings. A particular focus of the analysis is the relationship between medication adherence and variation in Part D benefits and cost sharing.

## **Data and Methods**

### **Data**

We used Surveillance, Epidemiology, and End Results (SEER) program cancer registry data, linked to Medicare administrative records (Warren, Klabunde, Schrag, Bach, & Riley, 2002). The National Cancer Institute's SEER program contracts with fifteen population-based cancer registries to provide data on all incident cancer cases (with the exceptions of non-melanoma

skin cancers and in situ cervical cancers) among residents of their reporting areas (Surveillance, Epidemiology, and End Results, 2010). At the time of the study, the program covered 26 percent of the U.S. population. For each reported case, SEER receives data on patient demographics, cancer site, month and year of diagnosis, extent of disease at diagnosis, and initial course of therapy (including cancer-directed surgery and radiation therapy). Clinical data contained in SEER permitted the identification of cancer patients who were appropriate candidates for endocrine therapy, along with the specific five year recommended timeframe for that therapy for each patient.

The SEER-Medicare database contains Medicare enrollment and claims files, including prescription drug event (PDE) records. PDE records, derived from prescription drug claims, contain information on the covered drugs, fill dates, total costs, patient out-of-pocket costs, and days' supply. Each record also indicates the benefit phase in which the claim was estimated to occur (deductible, pre-coverage gap, coverage gap, and catastrophic phase) based on chronological order of the enrollee's claims, total and out-of-pocket costs, and plan coverage (Chronic Condition Data Warehouse, 2011). PDE records are available for beneficiaries enrolled in both PDPs and MAPDs.

At the time of the study, SEER cases diagnosed through 2005 had been linked to Medicare records. Medicare claim and PDE records were available through 2007. We therefore examined SERM and AI use in 2006 and 2007 (the first two years of the Part D program) for cases diagnosed in years 2003–2005. This guaranteed that our observation period fell within the recommended five year timeframe for endocrine therapy, but it also created a time lag between diagnosis and the beginning of our observation period for endocrine therapy use. We were not able to determine what percentage of patients initiated endocrine therapy or to calculate utilization and adherence rates immediately following diagnosis. Our analysis, therefore, effectively focused on the use of endocrine therapy after the initial course of cancer treatment, and specifically within an approximately two-year window of time that began up to three years after diagnosis. This permitted us to compare utilization and adherence to therapy at various points within the five-year timeframe for endocrine therapy.

Medicare calculates for each beneficiary a Hierarchical Condition Category (HCC) risk score, based on diagnostic and demographic factors predictive of future Medicare costs (Pope et al., 2004). Risk scores for 2006 and 2007 were used in the analysis as a proxy for health status. We also obtained plan-level files that include various features of each Part D plan for 2007, such as the formulary tiers under which specific drugs were covered and whether any benefits were provided in the coverage gap for individual tiers. These plan-level files were not available for 2006.

## **Methods**

From SEER, we identified women diagnosed with invasive hormone receptor-positive (i.e., estrogen receptor- and/or progesterone receptor-positive) breast cancer in years 2003–2005 and

who underwent either mastectomy or breast conserving surgery (BCS). We excluded individuals identified through death certificate or autopsy, with unknown stage at diagnosis, with other cancers, and who spent more than 10 percent of their time in a hospital or skilled nursing facility (SNF) during the study period. The latter condition was imposed, because medications given to hospitalized patients are not identifiable from PDE records. Sample cases had to be age 65 or over and entitled to Medicare Part A and Part B as of January, 2006. From this initial sample, we identified women who had at least 12 months of Part D enrollment during the period of May 2006 to December 2007 (N=15,542). We excluded Part D enrollment in the period of January to April 2006, because initial implementation of the Part D program occurred during this period, and exploratory analyses of PDE records suggested possible undercounts, especially for LIS recipients. SERM and AI use was measured between May 2006 and December 2007.

To measure non-adherence to therapy, we identified the subset of sample members who had at least one PDE record for SERM or AI and who had at least 12 consecutive months of Part D enrollment following the first filled prescription for either drug. Non-adherence rates were computed separately for SERM and AI users, by LIS status; therefore, women who used both SERM and AI or who received the LIS for only part of the follow-up period, were excluded from the adherence analysis, yielding a final subset of 9,446 individuals. To calculate non-adherence rates, medication possession ratios (MPRs), consisting of total days' supply of the relevant drug divided by days of Part D enrollment, were computed for each case. The total days' supply was counted only up to the termination of Part D enrollment or December 31, 2007 (the end of the observation period). The denominator of the MPR was adjusted to remove days spent in a hospital or SNF. Consistent with common practice, cases with an MPR of less than 0.80 were defined as non-adherent (Kimmick et al., 2009; Partridge et al., 2003; Hershman et al., 2010).

To measure the variation in drug benefits among plans, we examined out-of-pocket costs associated with SERM and AI prescriptions. Specifically, we calculated average out-of-pocket costs per 30 days' supply of SERM or AI for each beneficiary without LIS, based on prescriptions filled before the coverage gap was reached. This captured the variation in plan cost-sharing policies in the pre-coverage gap period. To measure the effect of any benefits in the coverage gap on adherence, we used plan-level files to identify whether benefits were available in the coverage gap, for the most frequently prescribed SERM or AI, for each non-LIS Part D enrollee. For LIS recipients average out-of-pocket costs per 30 days' supply were calculated based on all prescriptions filled, because these individuals do not experience a coverage gap.

The analysis of utilization patterns and adherence included descriptive statistics and cross-tabulations. Logistic regression was used to identify factors associated with lack of treatment with endocrine therapy between May 2006 and December 2007, and specifically to determine whether utilization decreased with time from diagnosis. Logistic regression was also used to identify demographic, clinical, and Part D coverage characteristics associated with non-adherence to SERMs and AIs among women who had initiated endocrine therapy. We did not include chemotherapy use among our covariates, because it is not captured in SEER and

chemotherapy claims are not available for Medicare Advantage enrollees, who comprised a large portion of our sample. Analyses of non-adherence were stratified by LIS status after exploratory analyses revealed a strong interaction between LIS and out-of-pocket costs. Our primary analyses examined adherence among AI and SERM users separately, but we also pooled AI and SERM users (distinguishing them in the model with a binary variable) to compare non-adherence between the two drugs directly. All out-of-pocket costs incurred in 2006 were inflation-adjusted to 2007 dollars (Bureau of Labor Statistics, 2010).

A separate analysis was conducted of adherence to therapy during the coverage gap in 2007. From the 9,446 individuals identified for the adherence analysis, we selected enrollees without LIS who had at least one filled prescription for SERM or AI in the last quarter of 2006, who were enrolled in Part D for all of calendar year 2007, and who spent at least 30 days in the coverage gap in 2007. We then computed rates of non-adherence separately for time spent prior to the coverage gap and time spent in the coverage gap. Time spent in the catastrophic phase following the coverage gap was excluded from this analysis, because too few sample members had sufficient days in the catastrophic phase. LIS enrollees who incurred sufficient drug costs to reach the dollar threshold for the coverage gap, but who experienced no break in coverage, because of the LIS, were included in the analysis separately as a comparison. There were 5,436 individuals included in the analysis of adherence in the coverage gap.

## Results

### Utilization

During the period of May 2006–December 2007, 22 percent of beneficiaries received SERM, 52 percent received AI, and 26 percent received neither (Exhibit 1). Six percent of sample members received both SERM and AI and were classified in Exhibit 1 according to which drug they received first during the period of observation; among users of both drugs, 56 percent used SERM first and subsequently switched to AI (data not shown). Women diagnosed in 2005 were more likely to receive AIs during our observation period than women diagnosed in 2003 or 2004, consistent with reported trends toward greater use of AI among more recently diagnosed cases (Svahn et al., 2009; Aiello et al., 2008).

Lack of treatment with endocrine therapy was more common among women who were diagnosed in 2003 (odds ratio [OR] = 1.21, 95 percent confidence interval [CI] = [1.10, 1.33]) and 2004 (OR = 1.14, 95 percent CI = [1.04, 1.25]) than it was for those diagnosed in 2005 (Exhibit 2). Lack of treatment was most strongly associated with advanced age at diagnosis, white race, stage I disease, and receipt of BCS without adjuvant radiation therapy. Women with LIS were equally likely as women without LIS to forego endocrine therapy.

**Exhibit 1. Use of SERM and AI among elderly hormone receptor-positive female breast cancer patients enrolled in a Medicare Part D prescription drug plan, by patient characteristics, May 2006–December 2007.**

Characteristic	N	Percent using drug			p-value <sup>2</sup>
		SERM <sup>1</sup>	AI <sup>1</sup>	Neither	
All	15,542	22	52	26	
Part D benefit-related					
Part D low income subsidy					
No	11,848	23	51	27	< 0.001
Yes	3,694	21	55	24	
Plan type					
MAPD	6,186	23	51	26	0.10
PDP	9,356	22	52	26	
Demographic/health status					
Age at Part D enrollment					
65 - 69	3,673	20	60	20	
70 - 79	7,387	23	54	23	< 0.001
80 +	4,482	23	41	36	
Race/ethnicity					
White non-Hispanic	12,576	23	50	28	
White Hispanic	1,057	22	59	19	< 0.001
Black (non-Hisp. & Hisp.)	931	19	60	21	
Other/unknown <sup>3</sup>	978	23	57	20	
Married					
No/unknown <sup>3</sup>	8,483	22	50	28	< 0.001
Yes	7,059	23	53	24	
Urban/rural					
Large metro area	9,723	20	54	26	
Metro/urban	4,758	24	49	27	< 0.001
Less urban/rural	1,061	33	41	27	
Median income <sup>4</sup>					
< \$30K	2,004	25	52	24	
\$30K - \$49K	6,338	24	48	28	< 0.001
\$50K + / unknown <sup>3</sup>	7,200	20	55	25	
HCC risk score					
< = 1.00	7,450	23	50	27	
1.01 - 2.00	5,110	23	51	26	< 0.001
2.01 +	2,982	19	57	24	

Characteristic	N	Percent using drug			p-value <sup>2</sup>
		SERM <sup>1</sup>	AI <sup>1</sup>	Neither	
<b>Exhibit 1 (cont)</b>					
<b>Cancer-related</b>					
Year of diagnosis					
2003	4,823	27	45	28	
2004	5,320	22	51	27	< 0.001
2005	5,399	18	58	24	
Stage at diagnosis					
I	9,261	24	44	32	
II	5,022	21	61	18	< 0.001
III/IV	1,259	14	74	13	
Initial surgery/radiation					
Mastectomy	5,667	22	55	23	
BCS + radiation therapy	7,312	23	52	26	< 0.001
BCS, no radiation <sup>5</sup>	2,663	22	45	33	

<sup>1</sup> Beneficiaries receiving both SERM and AI were assigned to the drug with the earliest fill date during the observation period.

<sup>2</sup> p-value for difference between patient characteristic and utilization.

<sup>3</sup> Number of unknown cases varied from 2 (median income at census tract/ZIP Code level) to 361 (marital status).

<sup>4</sup> census tract/ZIP Code level

<sup>5</sup> includes unknown radiation therapy status

Notes:

- SERM = selective estrogen receptor modulator; AI=aromatase inhibitor; BCS=breast conserving surgery; MAPD=Medicare Advantage prescription drug plan; PDP=stand-alone prescription drug plan; HCC=Hierarchical Condition Category.
- Exhibit includes beneficiaries diagnosed between 2003 and 2005, with at least 12 months of Part D enrollment between May 2006 and December 2007.

Source: SEER-Medicare.



**Exhibit 2. Results of logistic regression model analyzing patient characteristics associated with lack of treatment with endocrine therapy among elderly hormone receptor-positive female breast cancer patients enrolled in a Medicare Part D prescription drug plan, May 2006 - December 2007**

Dependent variable: 1=no treatment, 0=treatment with SERM and/or AI

Characteristic	Odds ratio	95% CI
N	15,542	
<b>Part D benefit-related</b>		
Part D low income subsidy		
No	1.00	—
Yes	1.04	(0.94, 1.15)
Plan type		
PDP	1.00	—
MAPD	1.00	(0.92, 1.09)
<b>Demographic/health status</b>		
Age at Part D enrollment		
65 - 69	1.00	—
70 - 79	1.16	(1.05, 1.29) *
80 +	2.09	(1.87, 2.33) *
Race/ethnicity		
White non-Hispanic	1.00	—
White Hispanic	0.70	(0.59, 0.83) *
Black (non-Hisp. & Hisp.)	0.83	(0.70, 1.00) *
Other/unknown <sup>1</sup>	0.73	(0.61, 0.89) *
Married		
No/unknown <sup>1</sup>	1.00	—
Yes	0.83	(0.76, 0.89) *
Urban/rural		
Large metro area	1.00	—
Metro/urban	0.93	(0.83, 1.03)
Less urban/rural	0.81	(0.67, 0.98) *
Median income at census tract/ ZIP code level		
< \$30K	1.00	—
\$30K - \$49K	1.05	(0.92, 1.19)
\$50K + / unknown <sup>1</sup>	0.97	(0.84, 1.11)
HCC risk score		
< = 1.00	1.00	—
1.01 - 2.00	0.89	(0.82, 0.97) *
2.01 +	0.93	(0.83, 1.03)

**Exhibit 2 (cont)**

Characteristic	Odds ratio	95% CI
Cancer-related		
Year of diagnosis		
2003	1.21	(1.10, 1.33) *
2004	1.14	(1.04, 1.25) *
2005	1.00	—
Stage at diagnosis		
I	1.00	—
II	0.45	(0.41, 0.49) *
III/IV	0.30	(0.25, 0.36) *
Initial surgery/radiation		
Mastectomy	1.00	—
BCS + radiation therapy	0.93	(0.85, 1.01)
BCS, no radiation <sup>2</sup>	1.26	(1.13, 1.41) *

\* 95% confidence interval excludes 1.00.

<sup>1</sup> Number of unknown cases varied from 2 (median income at census tract/zip code level) to 361 (marital status).

<sup>2</sup> Includes unknown radiation therapy status.

## Notes:

- SERM = selective estrogen receptor modulator; AI = aromatase inhibitor; BCS=breast conserving surgery; MAPD=Medicare Advantage prescription drug plan; PDP=stand-alone prescription drug plan; HCC= Hierarchical Condition Category.
- Exhibit includes beneficiaries diagnosed between 2003 and 2005, with at least 12 months of Part D enrollment between May 2006 and December 2007.
- The model includes variables for each SEER registry and for number of months of Part D enrollment (data not shown in table).

Source: SEER-Medicare.

**Adherence**

Among SERM users 21 percent of non-LIS recipients and 24 percent of LIS recipients were non-adherent to therapy (Exhibit 3). Among AI users 30 percent of non-LIS recipients and 20 percent of LIS recipients were non-adherent. Adherence did not vary significantly with year of diagnosis, given some use of endocrine therapy in the observation period. Non-adherence increased significantly with increasing out-of-pocket costs for both LIS and non-LIS recipients, among both SERM and AI users. For example, among AI users without LIS, 10 percent of those with less than \$5 in out-of-pocket costs per 30 days' supply were non-adherent, compared to 33 percent of those with \$15 or more in out-of-pocket costs. Out-of-pocket costs varied less among LIS recipients than among non-LIS recipients, but adherence was still significantly better among those with lower out-of-pocket costs, among both SERM and AI users.

Logistic regression analysis confirmed the relationship between adherence and out-of-pocket costs, especially among non-LIS recipients (Exhibit 4). Among SERM users without LIS, the OR for non-adherence was 3.31 (95 percent CI = [2.14, 5.12]) for those with \$15 or more in

**Exhibit 3. Percent of elderly hormone receptor-positive female breast cancer patients enrolled in a Medicare Part D prescription drug plan who were non-adherent to SERM or AI therapy, by patient characteristics, May 2006–December 2007**

	Non-adherent to SERM						Non-Adherent to AI					
	Non-low income subsidy			Low income subsidy			Non-low income subsidy			Low income subsidy		
	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>
All	21	2,084		24	560		30	5,151		20	1,651	
Part D benefit-related												
Average out-of-pocket cost for 30 day supply <sup>2</sup>												
No Part D low income subsidy <sup>3</sup>												
\$0-\$4.99	17	666					10	317				
\$5.00-\$14.99	21	1,271	<0.001				12	479	<0.001			
\$15.00-\$29.99	35 <sup>5</sup>	135					33	2,245				
\$30.00+	—						34	2,053				
Part D low income subsidy												
\$0-\$1.99				22	465	0.008				16	649	
\$2.00-\$4.99				35 <sup>6</sup>	95					21	710	<0.001
\$5.00+				—						26	292	
Coverage gap benefits												
No	20	1,718	0.35	—			30	5,046	0.10	—		
Yes	23	366		—			23	105		—		
Plan type												
MAPD	21	970	0.87	33	116	0.01	26	2,369	<0.001	19	269	0.64
PDP	21	1,114		22	444		33	2,782		20	1,382	
Demographic/health status												
Age at Part D enrollment												
65-69	20	394		27	119		29	1,468		20	435	
70-79	19	1,046	0.09	24	259	0.62	30	2,561	0.49	19	801	0.83
80+	24	644		22	182		31	1,122		21	415	

Exhibit 3 (cont)	Non-adherent to SERM						Non-Adherent to AI					
	Non-low income subsidy			Low income subsidy			Non-low income subsidy			Low income subsidy		
	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>
Race/ethnicity												
White non-Hispanic	21	1,823		22	355		30	4,401		18	960	
White Hispanic	28	97	0.001	25	77	0.46	32	272	0.04	21	266	0.05
Black (non-Hisp. & Hisp.)	37	51		31	75		37	214		26	252	
Other/unknown	12	113		26	53		25	264		19	173	
Married												
No/unknown	21	975	0.55	24	438	0.70	33	2,335	<0.001	20	1,253	0.72
Yes	20	1,109		25	122		28	2,816		21	398	
Urban/rural												
Large metro area	21	1,188		27	301		28	3,546		19	975	
Metro/urban	21	695	0.34	22	176	0.11	34	1,386	<0.001	23	533	0.12
Less urban/rural	17	201		17	83		37	219		16	143	
Median income at census tract/ ZIP Code level												
<\$30K	19	216		30	166		34	395		23	468	
\$30K-\$49K	21	921	0.84	19	273	0.01	32	1,825	0.001	22	717	0.002
\$50K+/unknown	21	947		29	121		28	2,931		15	466	
HCC risk score												
<=1.00	18	1,125		29	181		29	2,707		18	455	
1.01-2.00	22	687	0.002	21	236	0.17	30	1,561	0.15	19	648	0.20
2.01+	28	272		24	143		33	883		22	548	
Cancer-related												
Year of diagnosis												
2003	19	779		24	221		31	1,411		20	431	
2004	21	695	0.39	28	181	0.29	30	1,744	0.56	23	577	0.07
2005	22	610		20	158		30	1,996		17	643	

Exhibit 3 (cont)	Non-adherent to SERM						Non-Adherent to AI					
	Non-low income subsidy			Low income subsidy			Non-low income subsidy			Low income subsidy		
	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>	Percent	N	p-value <sup>1</sup>
Stage at diagnosis												
I	21	1,412		22	293		30	2,768		17	712	
II	20	596	0.11	25	225	0.40	30	1,885	0.78	22	683	0.06
III/IV	30	76		31	42		31	498		22	256	
Initial surgery/radiation												
Mastectomy	20	672		23	257		30	1,756		20	800	
BCS+radiation	21	1,054	0.91	26	200	0.72	29	2,655	0.04	20	587	1.00
BCS, no radiation <sup>4</sup>	21	358		22	103		34	740		20	264	

<sup>1</sup>p-value for difference between patient characteristic and non-adherence.

<sup>2</sup>Prior to the coverage gap.

<sup>3</sup>Excludes 12 SERM and 57 AI cases with no pre-coverage gap claims.

<sup>4</sup>Includes unknown radiation therapy status.

<sup>5</sup>Includes 22 cases with out-of-pocket costs of \$30+.

<sup>6</sup>Includes 11 cases with out-of-pocket costs of \$5+.

Notes:

- SERM = selective estrogen receptor modulator; AI = aromatase inhibitor; BCS=breast conserving surgery; MAPD=Medicare Advantage prescription drug plan; PDP=stand-alone prescription drug plan; HCC= Hierarchical Condition Category.
- Table includes beneficiaries diagnosed between 2003 and 2005 with at least 12 months of Part D enrollment between May 2006 and December 2007. Cases with both AI and SERM were excluded from this analysis.
- Non-adherence is defined as a medication possession ratio of less than 80 percent.

Source: SEER-Medicare.

**Exhibit 4. Results of four logistic regression models analyzing patient characteristics associated with non-adherence to SERM or AI therapy among elderly hormone receptor-positive female breast cancer patients enrolled in a Medicare Part D prescription drug plan, May 2006 - December 2007**

Dependent variable: 1=non-adherent; 0=adherent	SERM				AI			
	Non-low income subsidy		Low income subsidy		Non-low income subsidy		Low income subsidy	
N	2,072		560		5,094		1,651	
Independent variable	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Part D benefit-related								
Average out-of-pocket cost for 30 day supply <sup>1</sup>								
No Part D low income subsidy								
\$0 - \$4.99	1.00	—			1.00	—		
\$5.00 - \$14.99	1.41	(1.09, 1.82)			1.24	(0.78, 1.96)		
\$15.00 - \$29.99	3.31 <sup>2</sup>	(2.14, 5.12)			4.52	(3.05, 6.69)		
\$30.00 +		—			4.47	(3.02, 6.61)		
Part D low income subsidy								
\$0 - \$1.99			1.00	—			1.00	—
\$2.00 - \$4.99			2.15 <sup>3</sup>	(1.25, 3.71)			1.37	(1.03, 1.84)
\$5.00+				—			2.00	(1.37, 2.93)
Coverage gap benefits	1.16	(0.87, 1.55)			0.60	(0.37, 0.97)		
Plan type								
MAPD	1.12	(0.85, 1.47)	1.46	(0.87, 2.43)	0.93	(0.80, 1.08)	0.97	(0.68, 1.39)
PDP	1.00	—	1.00	—	1.00	—	1.00	—
Demographic/health status								
Age at Part D enrollment								
65 - 69	1.00	—	1.00	—	1.00	—	1.00	—
70 - 79	0.88	(0.65, 1.20)	0.94	(0.55, 1.60)	1.05	(0.90, 1.22)	0.97	(0.72, 1.31)
80 +	1.15	(0.82, 1.61)	0.87	(0.48, 1.58)	0.99	(0.82, 1.20)	1.09	(0.76, 1.55)

Exhibit 4 (cont)	SERM				AI			
	Non-low income subsidy		Low income subsidy		Non-low income subsidy		Low income subsidy	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Race/ethnicity								
White non-Hispanic	1.00	—	1.00	—	1.00	—	1.00	—
White Hispanic	1.38	(0.83, 2.28)	0.81	(0.42, 1.58)	1.31	(0.98, 1.74)	1.17	(0.79, 1.72)
Black (non-Hisp. & Hisp.)	2.60	(1.39, 4.87)	1.23	(0.62, 2.43)	1.86	(1.35, 2.55)	1.41	(0.96, 2.06)
Other/unknown	0.62	(0.33, 1.20)	0.79	(0.36, 1.75)	1.00	(0.72, 1.40)	1.25	(0.77, 2.04)
Married	1.02	(0.82, 1.28)	1.07	(0.64, 1.78)	0.77	(0.68, 0.88)	1.09	(0.81, 1.48)
Urban/rural								
Large metro area	1.00	—	1.00	—	1.00	—	1.00	—
Metro/urban	0.98	(0.72, 1.35)	0.93	(0.50, 1.75)	1.11	(0.93, 1.34)	1.20	(0.83, 1.73)
Less urban/rural	0.86	(0.51, 1.47)	0.64	(0.25, 1.60)	1.15	(0.80, 1.64)	0.69	(0.37, 1.31)
Median income at census tract/ZIP Code level								
< \$30K	1.00	—	1.00	—	1.00	—	1.00	—
\$30K - \$49K	1.11	(0.74, 1.65)	0.44	(0.25, 0.75)	1.01	(0.79, 1.30)	1.01	(0.74, 1.39)
\$50K + / unknown	1.08	(0.71, 1.65)	0.66	(0.34, 1.27)	0.90	(0.70, 1.16)	0.68	(0.46, 1.01)
HCC risk score								
< = 1.00	1.00	—	1.00	—	1.00	—	1.00	—
1.01 - 2.00	1.19	(0.93, 1.53)	0.64	(0.39, 1.04)	1.04	(0.90, 1.21)	1.16	(0.84, 1.60)
2.01 +	1.73	(1.24, 2.40)	0.79	(0.45, 1.37)	1.15	(0.96, 1.38)	1.47	(1.05, 2.07)
Cancer-related								
Year of diagnosis								
2003	0.86	(0.65, 1.13)	1.09	(0.64, 1.86)	1.13	(0.97, 1.32)	1.21	(0.88, 1.68)
2004	0.97	(0.74, 1.27)	1.26	(0.72, 2.21)	1.02	(0.88, 1.18)	1.36	(1.01, 1.82)
2005	1.00	—	1.00	—	1.00	—	1.00	—

<b>Exhibit 4 (cont)</b>	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Stage at diagnosis								
I	1.00	—	1.00	—	1.00	—	1.00	—
II	0.91	(0.71, 1.18)	1.27	(0.81, 1.99)	0.94	(0.82, 1.08)	1.35	(1.02, 1.78)
III/IV	1.54	(0.89, 2.68)	1.71	(0.76, 3.87)	1.00	(0.79, 1.26)	1.29	(0.87, 1.92)
Initial course of therapy								
Mastectomy	1.00	—	1.00	—	1.00	—	1.00	—
BCS + radiation	1.10	(0.84, 1.44)	1.11	(0.67, 1.82)	0.98	(0.84, 1.14)	1.15	(0.85, 1.54)
BCS, no radiation <sup>4</sup>	0.91	(0.65, 1.29)	0.93	(0.50, 1.73)	1.22	(1.00, 1.49)	1.10	(0.76, 1.59)

<sup>1</sup>Prior to the coverage gap.

<sup>2</sup>Includes 22 cases with out-of-pocket costs of \$30+.

<sup>3</sup>Includes 11 cases with out-of-pocket costs of \$5+.

<sup>4</sup> Includes unknown radiation therapy status.

Notes:

- SERM = selective estrogen receptor modulator; AI = aromatase inhibitor; BCS=breast conserving surgery; MAPD=Medicare Advantage prescription drug plan; PDP=stand-alone prescription drug plan; CI=confidence interval; HCC=Hierarchical Condition Category.
- Table includes beneficiaries diagnosed between 2003 and 2005 with at least 12 months of Part D enrollment between May 2006 and December 2007. • Cases with both AI and SERM were excluded from this analysis.
- The models exclude 12 SERM and 57 AI non-low income subsidy cases with no pre-coverage gap claims.
- Non-adherence is defined as a medication possession ratio of less than 80 percent.
- The model also includes variables for each SEER registry (data not shown in table).

Source: SEER-Medicare.



out-of-pocket costs per 30 days' supply compared to those with less than \$5 in out-of-pocket costs. The comparable OR for AI users was 4.52 (95 percent CI = [3.05, 6.69]). The relationship between adherence and out-of-pocket costs was not as strong for LIS recipients. Among AI users without LIS, adherence was significantly better for those with benefits in the coverage gap for their most frequently prescribed AI (OR for non-adherence = 0.60, 95 percent CI = [0.37, 0.97]). Adherence was poorer among black beneficiaries without LIS for both SERM and AI. High risk scores were associated with poorer adherence for SERM users without LIS and for AI users with LIS.

The strong relationship between out-of-pocket costs and adherence suggests that the poorer adherence associated with AI users without LIS may be attributable to the higher cost of AI to the beneficiary. After pooling SERM and AI users without LIS, AI users were shown to be more likely to be non-adherent, controlling for demographic, health status, and cancer-related factors (OR = 1.67, 95 percent CI = [1.47, 1.90]; data not shown). After further adjusting for out-of-pocket costs and the presence of benefits in the coverage gap, AI users were less likely to be non-adherent (OR = 0.63, 95 percent CI = [0.51, 0.78]).

Adherence deteriorated among AI users who entered the coverage gap (Exhibit 5). Among AI users without LIS, 13.4 percent were non-adherent prior to the coverage gap, with 25.3 percent non-adherent during time spent in the coverage gap. SERM users without LIS experienced non-significantly poorer adherence after entering the coverage gap. By comparison, LIS recipients, who suffered no break in coverage, experienced a small non-significant improvement in adherence after the coverage gap threshold was reached.

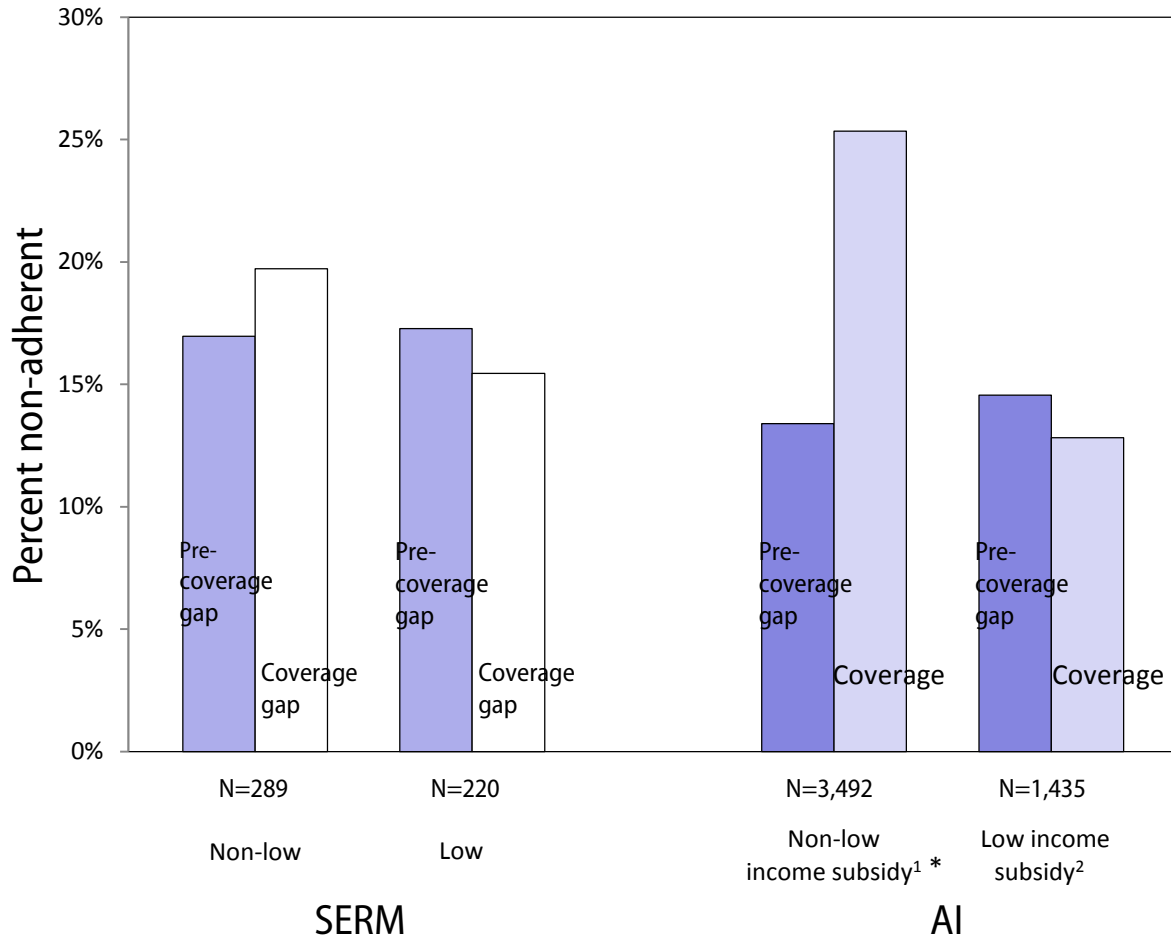
## Discussion

Our findings present a mixed view of utilization and adherence patterns for AI and SERM under Part D. Although most women were receiving some endocrine therapy during the 20 months of our study, a significant minority were not. Among those receiving therapy, a substantial number was non-adherent, especially among AI users. Higher out-of-pocket costs were strongly associated with non-adherence to therapy for both AI and SERM users, and among both LIS and non-LIS recipients. We also observed a significant deterioration in adherence during the coverage gap among AI users.

Of the elderly women with Part D coverage who had hormone receptor-positive breast cancer, 26 percent were not receiving SERM or AI therapy between one and five years after diagnosis, a period when endocrine therapy is recommended for all patients. As time from diagnosis increased, use of endocrine therapy decreased. A prior study of a sample of SEER cases diagnosed in 2000 found approximately 28 percent of women with ER-positive breast cancers did not receive tamoxifen as part of initial therapy (Harlan, Clegg, Abrams, Stevens, & Ballard-Barbash, 2006). Studies based on other populations have found that 20-50 percent of SERM and AI users fill too few prescriptions to provide an adequate days' supply of their drug or they

discontinue therapy early, with lack of treatment tending to increase with time from diagnosis (Partridge et al., 2003; Owusu et al., 2008; Lash et al., 2006; Chlebowski & Geller, 2006; Hershman et al., 2010; Partridge et al., 2008). Reasons for lack of treatment include side effects, patient attitudes and beliefs, duration of therapy, out-of-pocket costs, and patient experiences

**Exhibit 5. Rates of non-adherence for SERM and AI among elderly hormone receptor-positive female breast cancer patients enrolled in a Medicare Part D prescription drug plan who reached the coverage gap in 2007, by benefit phase**



\* p < 0.05 for difference between pre-coverage gap and coverage gap.

<sup>1</sup>Excludes enrollees with benefits in the coverage gap.

<sup>2</sup>Enrollees incurred sufficient drug costs to reach the coverage gap but continued to receive Part D benefits thereafter under the low income subsidy.

Notes:

- SERM=selective estrogen receptor modulator; AI=aromatase inhibitor.
- Table includes beneficiaries diagnosed between 2003 and 2005, with at least one Part D claim for SERM or AI in the last quarter of 2006, who were enrolled in a Part D plan for all of calendar 2007 and who reached the coverage gap in 2007.
- Excludes enrollees with less than 30 days in the coverage gap.
- Cases with both AI and SERM use were excluded from this analysis.

Source: SEER-Medicare.

with care (Kahn, Schneider, Malin, Adams, & Epstein, 2007; Chlebowski & Geller, 2006; Hadji, 2010). Despite the variation in Part D benefits and the presence of a coverage gap for most enrollees, utilization of endocrine therapy under Part D appears comparable to utilization rates observed in other settings.

We found significantly lower medication adherence among enrollees who experienced higher out-of-pocket costs, especially among AI users. This suggests that differences in plan cost sharing have important implications for enrollee access to essential medications. Other research has indicated that most beneficiaries do not select Part D plans that minimize their out-of-pocket costs for their medications (Gruber, 2009; Patel et al., 2009). Many have a poor understanding of the Part D program and most do not compare plan cost and benefits in their enrollment decisions (Hibbard, Greene, & Tusler, 2006). Enrollees are also reluctant to switch plans, even if it would improve their benefits (Polinski, Bhandari, Saya, Schneeweiss, & Shrank, 2010). In particular, LIS recipients, many of whom are initially randomly assigned to selected plans, may improve access by switching to more appropriate plans (United States Government Accountability Office, 2007).

We found evidence that the Part D coverage gap may adversely affect adherence among AI users without LIS. Adherence was significantly better for AI users who had some coverage for their AI drug during the coverage gap phase, although the same did not hold true for SERM users. In addition, adherence deteriorated significantly among AI users after the coverage gap was reached. The effect of the coverage gap on adherence may be understated in our data if some enrollees discontinue therapy before entering the coverage gap, in anticipation of encountering much higher out-of-pocket costs. Any effect of the coverage gap on adherence may be mitigated over time as the coverage gap is phased out of the Part D program (Centers for Medicare & Medicaid Services, 2010).

Among women receiving endocrine therapy, we found higher rates of non-adherence among AI users than among SERM users for beneficiaries without LIS. Previous studies based on clinical trials and observational data have found non-adherence rates to be similar for these two classes of drugs (Chlebowski & Geller, 2006; Hershman et al., 2010). Our findings suggest the poorer adherence among AI users that we observed may be attributable to the higher out-of-pocket costs associated with that class of drugs under Part D. Large differences in out-of-pocket costs between SERMs and AIs result in part from the structure of the standard Part D benefit, which imposes a deductible, a 25 percent coinsurance rate, and a coverage gap during which patients are responsible for the full cost of their drugs. Most Part D plans that provided benefits in the coverage gap in years 2006–2007 did so only for generic drugs (Hargrave, Hoadley, Cubanski, & Neuman, 2009), providing little relief for AI users. The utilization restrictions placed on higher tier drugs (e.g., quantity limits, prior authorization) may also affect adherence for AI users. If AIs continue to displace SERMs as they have in recent years, adherence to endocrine therapy could worsen over time among beneficiaries without LIS.

Dually eligible beneficiaries (individuals with both Medicare and Medicaid coverage) have historically received drug coverage through the Medicaid program, but under Part D most of their drug coverage is now provided by Medicare. Previous studies have found substantial rates of non-adherence to endocrine therapy among Medicaid recipients with breast cancer (Kimmick et al., 2009; Partridge et al., 2003). Concerns have been expressed that the transition to Medicare drug coverage may have created financial barriers to the receipt of needed medications for many dual eligibles through greater cost sharing or formulary restrictions (Elliott, Majumdar, Gillick, & Soumerai, 2005). Although we could not observe drug utilization patterns of dual eligibles prior to coverage under Part D, we did compare utilization and adherence rates for endocrine therapy between LIS recipients (who are comprised mostly of dual eligibles) and non-LIS recipients under Part D. Similar percentages of LIS and non-LIS enrollees received endocrine therapy and similar percentages received AIs, which are more expensive than SERMs. Moreover, among AI users adherence rates were significantly higher for LIS recipients than for non-LIS recipients. Access to endocrine therapy, therefore, appears to be as good for dual eligibles as for other beneficiaries. Our findings are consistent with other studies that have found few problems with the transition of drug coverage for dual eligibles from Medicaid to Part D (Polinski, Kilabuk, Schneeweiss, Brennan, & Shrank, 2010).

Several limitations of this study should be noted. First, we could not observe SERM and AI use from time of diagnosis, when endocrine therapy is recommended to commence. However, our study included an interval when all patients should have been receiving endocrine therapy. Second, our analyses of factors related to utilization and adherence could not account for side effects, which are an important reason for non-adherence and discontinuation of these drugs (Chlebowski & Geller, 2006). Third, our sample was limited to Part D enrollees, who tend to be less healthy and have lower incomes than non-Part D enrollees (Riley, Levy, & Montgomery, 2009). Fourth, some of our findings could be explained by biased selection of beneficiaries into plans with different cost sharing and benefit packages (Riley, et. al, 2009). That is, beneficiaries who make the effort to enroll in plans that minimize cost-sharing for endocrine therapy drugs may also tend to be more meticulous about remaining adherent to therapy. Lastly, we could not be certain that our database captured all prescription fills for our sample. For example, some beneficiaries may obtain free sample medications from their doctors or receive their drugs through other sources that would not show up in PDE records, particularly during the coverage gap. Despite the study limitations, this analysis represents the first use of Medicare Part D records incorporated into the SEER-Medicare database, demonstrating the potential value of the data for studying prescription drug use among elderly cancer patients.

We conclude that under Part D, most elderly women with breast cancer who could benefit from endocrine therapy are receiving recommended treatment. However, a sizeable proportion is not receiving endocrine therapy in the recommended time frame following their diagnosis. In addition, among those women initiating endocrine therapy, about one-quarter was non-adherent, with out-of-pocket costs appearing to be a significant factor. Failure to initiate

treatment with SERM or AI and poor adherence during the five years of recommended therapy can diminish the important role that endocrine therapy plays in reducing recurrences in women with breast cancer. Although Part D provides important access to medications for Medicare beneficiaries, there may still be barriers that prevent some beneficiaries from receiving care.

### **Correspondence**

Gerald F. Riley, M.S.P.H., U.S. DHHS, Centers for Medicare & Medicaid Services, 7500 Security Blvd., Mailstop WB-06-05 Baltimore, MD 21244 [gerald.riley@cms.hhs.gov](mailto:gerald.riley@cms.hhs.gov), Tel: 410-786-6699, Fax: 410-786-5515

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