

Impact of Formulary Restrictions on Medication Use and Costs

Xian Shen, PhD; Bruce C. Stuart, PhD; Christopher A. Powers, PharmD; Sarah E. Tom, PhD, MPH; Laurence S. Magder, PhD; and Eleanor M. Perfetto, PhD, MS

More than 30 million Medicare beneficiaries obtain prescription drug coverage through Part D each year.¹ Although CMS requires Part D plans to include at least 2 drugs from each therapeutic class on their formulary, coverage of specific drugs may differ across plans. In 2010, some plans covered all drugs from the CMS drug reference file whereas other plans included as few as 63% of those drugs.² Variation in coverage occurred not only to multisource brand name drugs, but also to single-source medications widely used by Medicare beneficiaries. In 2012, 5 of the 10 most frequently prescribed brand name drugs among Medicare beneficiaries were unavailable or excluded from formulary for more than 5% of all beneficiaries enrolled in stand alone prescription drug plans (PDPs).³ Furthermore, use of prior authorization (PA) among covered drugs increased from 8% in 2007 to 20% in 2012.³

Formulary noncoverage and utilization management (UM) tools (eg, PA, step therapy [STEP]) are intended to facilitate the efficient use of medications and contain prescription drug costs. Under the Medicare Part D program, an enrollee, an enrollee's representative, or an enrollee's prescriber can request that the plan sponsor make a formulary exception or determine whether the enrollee has satisfied a UM requirement. This process is called coverage determination.⁴ If a plan sponsor issues an unfavorable coverage determination, the decision may be appealed through the Part D appeals process. In the standard process, the adjudication timeframe is 72 hours for a coverage determination and 7 days for the first appeal.⁵ Prior research suggests that many beneficiaries, particularly those with low socioeconomic status, have difficulty navigating their Part D benefit and understanding the coverage determination and exception process.^{6,7} These challenges may present hurdles for beneficiaries to obtain and adhere to the medications prescribed to them. However, little is known regarding the impact of noncoverage, PA, and STEP—collectively referred to as "formulary restrictions" in this paper—on medication utilization and costs and whether those formulary restrictions may cause unintended reduction in overall medication adherence.

ABSTRACT

OBJECTIVES: To evaluate the effects of formulary restrictions on utilization and costs of oral hypoglycemic agents (OHAs), statins, and renin-angiotensin system (RAS) antagonists among low-income subsidy (LIS) recipients in Medicare Part D plans.

STUDY DESIGN: We analyzed a 5% sample of 2012 Medicare data from the Chronic Conditions Data Warehouse together with a customized dataset capturing beneficiaries' histories of plan assignment.

METHODS: We constructed 3 nonexclusive study cohorts comprising of users of OHAs, statins, and RAS antagonists. Eligible study subjects were LIS recipients randomized to benchmark plans. Formulary restrictions of interest were noncoverage, prior authorization, and step therapy. Study outcomes included generic dispensing rate (GDR), mean cost per prescription fill, and medication adherence based on proportion of days covered (PDC). Random intercept regression models were performed to estimate the effects of formulary restrictions on the study outcomes by drug class.

RESULTS: After covariate adjustment, beneficiaries who were subject to formulary restrictions on brand name pioglitazone and single-source brand name dipeptidyl peptidase-4 inhibitors (saxagliptin, sitagliptin, and sitagliptin-metformin) had a GDR 3 percentage points higher and a cost per prescription fill \$10.8 less, but similar PDC compared with those who faced no restrictions. Restricting access to brand name atorvastatin and single-source brand name statins (rosuvastatin and ezetimibe-simvastatin) was associated with a GDR 14.9 percentage points higher and a cost per prescription fill \$29.6 less, but with no impact on PDC. Restricting use of single-source brand name RAS antagonists (olmesartan, valsartan, and valsartan-hydrochlorothiazide) was associated with a GDR 15.0 percentage points higher, a cost per prescription fill \$27.2 less, and a PDC 1.3 percentage points lower.

CONCLUSIONS: Placing formulary restrictions on brand name drugs shifts utilization toward generic drugs, lowers the overall cost per prescription fill, and has minimal impact on overall adherence for OHAs, statins, and RAS antagonists among LIS recipients.

Am J Manag Care. 2017;23(8):e265-e274

TAKEAWAY POINTS

Formulary restrictions—noncoverage, prior authorization, and step therapy—are increasingly employed by Medicare Part D plans to manage medication utilization and costs. This study evaluated the effects of formulary restrictions on utilization and costs of oral hypoglycemic agents (OHAs), statins, and renin-angiotensin system (RAS) antagonists among randomized low-income subsidy (LIS) recipients.

- ▶ Benchmark Part D plans tend to make generic drugs readily available on formulary and place restrictions on brand name drugs.
- ▶ Formulary restrictions on brand name drugs shift utilization toward generic drugs, lower cost per prescription fill, and have minimal impact on overall adherence for OHAs, statins, and RAS antagonists among LIS recipients.

Two analytic challenges exist in bridging this knowledge gap. First, plans often impose formulary restrictions—either together or complementarily with cost-sharing rules—to control medication utilization and costs; thus, it is analytically complex to isolate the effects of one from the other. Second, factors that influence beneficiaries' selection of PDPs (eg, health beliefs, risk preferences, and expectations for medication needs) are typically unobservable, but may bias estimates of plan effects.

Our study addressed these 2 analytic challenges by exploiting a natural experiment in which CMS randomly assigned beneficiaries receiving low-income subsidies (LIS) to benchmark PDPs within regions.^{4,5} More than 90% of all LIS recipients received a full subsidy and paid the same nominal co-pays for prescription drugs regardless of plan cost-sharing rules.^{8,9} Hence, focusing the analysis on LIS recipients allowed evaluation of the effects of formulary restrictions, independent of plans' cost-sharing rules. To further ensure that LIS recipients had affordable prescription drug coverage, CMS randomly assigned those who did not voluntarily select a Part D plan to one of the benchmark PDPs in their region. Each year, CMS also reassigns LIS recipients from plans that are terminating or charging premiums above regional benchmark thresholds.^{4,5,10} Randomization is expected to balance both observable and unobservable beneficiary characteristics among plans, thus creating a unique research opportunity for understanding how formulary restrictions affect medication utilization and costs.

Our study focused on 3 classes of medications commonly used by Medicare beneficiaries: oral hypoglycemic agents (OHAs), statins, and renin-angiotensin system (RAS) antagonists. Adherence outcomes for these 3 drug classes were included as quality measures in the Medicare Star Ratings program and assigned the highest weight in calculating overall Stars. Recent CMS investigations have revealed that receipt of LIS is associated with poorer outcomes for several Star measures, including suboptimal adherence for OHAs, statins, and RAS antagonists.^{11,12} Findings from this study can also provide Part D plans with valuable insights regarding the extent to which lifting formulary restrictions may improve LIS recipients' medication adherence for the 3 drug classes.

METHODS

Data Source

We analyzed a 5% sample of 2012 Medicare data from the Chronic Conditions Data Warehouse (CCW). The CCW formulary file provided detailed information regarding formulary restrictions for the drugs of interest in 2012. The CCW prescription drug event file contained claims for prescription drugs incurred by beneficiaries during the year, as well as information on Part D plan character-

istics and beneficiaries' utilization of inpatient, outpatient, and physician services. More details about the CCW data files can be found elsewhere.¹³ In addition, we obtained a customized dataset from CMS that captured beneficiaries' histories of plan assignment, dating back to 2006. Through this file, we were able to identify LIS recipients who were randomly assigned to benchmark PDPs by CMS and who remained in their assigned plan as of January 1, 2012.

Study Cohorts

We constructed 3 nonexclusive study cohorts comprising users of OHAs, statins, and RAS antagonists. Eligible study beneficiaries must have been continuously enrolled in Medicare Parts A, B, and D throughout calendar year 2012 and have received LIS throughout 2012. In addition, eligible beneficiaries for a particular cohort must have had at least 2 prescription fills for the drugs of interest included in the study in 2012. We excluded beneficiaries who made plan choices prior to 2012, but allowed those who switched plans in mid-year 2012 to remain in the data analysis according to the intention-to-approach commonly used in clinical trials. For technical reasons detailed below, we also excluded beneficiaries enrolled in 1 Part D contract (ie, Envision RxPlus Silver; Twinsburg, Ohio) from the analysis.

Measures

The 3 outcome measures were generic dispensing rate (GDR), mean cost per prescription fill, and medication adherence based on the proportion of days covered (PDC) by any drugs in the class. GDR was calculated as annual days of supply for generics divided by annual total days of supply for all drugs in the class. Mean cost per prescription fill was determined by dividing the total drug expenditure by the total prescription fills for all drugs in the class. PDC was computed by dividing days covered by total observation days. Days covered by overlapping prescriptions for the same drug were adjusted by rolling over the overlapping days to cover later days when lack of drug supply was identified. Similarly, days covered during inpatient stays were applied to subsequent days with no drug supply. Days in inpatient facilities were removed from both the numerator and the denominator of PDC.⁸ PDC was capped at 1.

In our assessment of formulary restrictions, we only considered drugs accounting for at least 1% of overall utilization of the drug class in all LIS recipients. Among those drugs, the scope of analysis was further narrowed down to those with varying degrees of restriction across the benchmark PDPs in 2012. The rationale behind these 2 requirements was that the impact of formulary restriction of a specific drug cannot be detected unless the drug was prescribed in the study population and its access was restricted to different degrees across plans.

Formulary restrictions of interest were noncoverage (ie, off formulary), PA, and STEP. To identify off-formulary medications, we first identified all drug products from the drug lists used by the Medicare Star Ratings program and then cross-checked to see exclusions to each plan.^{12,14} Indicators for PA and STEP were available from the CCW formulary file. We measured the degree of restriction for each drug identified at the brand level versus the generic and dosage-form levels, which allowed us to examine how restricting access to the brand name version of a multi-source drug or specific dosage forms might impact study outcomes. The degree of restriction for a drug was categorized as: 1) none restricted, if no strengths of that drug were subject to noncoverage, PA, or STEP; 2) partially restricted, if at least 1, but not all, strengths of the drug were subject to noncoverage, PA, or STEP; and 3) all restricted, if all strengths of the drug were subject to noncoverage, PA, or STEP.

Notably, we observed perfect correlations in the degree of restriction among drugs in each of the 3 classes. Specifically, every plan that partially restricted generic simvastatin also partially restricted ezetimibe-simvastatin. Plans either fully restricted brand name pioglitazone, sitagliptin, and sitagliptin-metformin across the board or did not restrict any of the 3 drugs. Plans that fully restricted valsartan also fully restricted valsartan-hydrochlorothiazide. We constructed composite measures that grouped commonly occurring formulary restrictions and estimated the effects of each group on the study outcomes. **Table 1** provides a list of drugs selected for analysis, the degrees of restriction observed, and groups of formulary restrictions formed (**eAppendix Table 1** displays formulary restrictions on individual drugs [eAppendices available at ajmc.com]). As indicated in the table, 3 OHA (sitagliptin, sitagliptin-metformin, saxagliptin), 2 statins (ezetimibe-simvastatin, rosuvastatin), and 3 RAS antagonists (olmesartan, valsartan all, valsartan-hydrochlorothiazide) were single-source drugs for which generics were unavailable in 2012.

Key covariates included a variable for count of generics available without charge via mail order, indicators for PDP regions, and a categorical variable representing state laws for generic substitution. Plan cost-sharing rules are generally not applicable to full LIS recipients as they pay flat co-pays for prescription drugs (at most \$2.60 for generics and \$6.50 for brand name drugs in 2012).⁸ However, in 2012, several plans provided free mail order prescriptions for commonly used generics in the 3 drug classes of interest.

The covariate—the count of generics available for free via mail order—was developed to account for the effect of this practice at the plan level. Last, several PDP regions covered multiple states, some of which could have had more forceful state laws for generic substitution than others. To represent the strictness of the state laws, we constructed a categorical variable consisting of 3 values: 1) state law allows generic substitution, 2) state law mandates generic substitution but allows brand by patient request, and 3) state law mandates generic substitution but allows brand by provider request.

We also evaluated the impact of CMS assignment methods by comparing enrollee characteristics across the benchmark PDPs within each of the 3 largest PDP regions: New York, Texas, and California. We expected comparable enrollee characteristics between plans, except for assignment year and age because some plans had operated as benchmark plans for more years and, thus, would have received more random assignees compared with plans that achieved benchmark status in recent years. These older benchmark plans would also have retained an older pool of enrollees. Beneficiary age and assignment year were also included as covariates in the analysis.

Statistical Analysis

In univariate analysis, we performed type 3 tests to examine the overall effect of the composite groups of formulary restrictions on each study outcome. We estimated 3 sets of random intercept regression models in which dependent variables were GDR, mean cost per prescription fill, and PDC. In each regression model, we included a random effect to account for unexplained variability between plans. Formulary restrictions were modeled as fixed effects. Count of generics available without charge via mail order, state law for generic substitution, PDP region, assignment year, and beneficiary age were included as covariates in the models and treated as fixed effects. We used SAS Version 9.3 (SAS Institute; Cary, North Carolina) for all statistical analyses.

RESULTS

A total of 28,082 beneficiaries were eligible for the OHA cohort; 53,864 for the statin cohort; and 57,289 for the RAS antagonist cohort (see **eAppendix Figure** for details about cohort selection). Approximately 30% of all study subjects resided in New York, Texas, and California in 2012 (**eAppendix Table 2**). As expected, enrollee characteristics were largely comparable across benchmark PDPs within each of these 3 regions except for assignment year and age (**eAppendix Tables 3-11**).

From our assessment of the benchmark PDP formulary designs in 2012, we found consistent patterns in formulary restrictions for OHAs, statins, and RAS antagonists. For most of the drugs analyzed, plans either fully restricted their use (all strengths restricted) or applied no restrictions at all (all strengths available). Formulary

TABLE 1. Identification of Eligible Drugs and Groups of Formulary Restrictions

Drug Class	Drugs Accounting for ≥1% of Overall Utilization	Drugs Eligible for Analysis (observed degrees of restriction)	Groups of Formulary Restrictions
OHAs	<ul style="list-style-type: none"> • Generic glimepiride • Generic glipizide • Generic glipizide XL • Generic glipizide ER • Generic glyburide • Generic glyburide-metformin • Generic metformin • Generic pioglitazone • Brand name pioglitazone • Sitagliptin^a • Sitagliptin-metformin^a • Saxagliptin^a 	<ul style="list-style-type: none"> • Brand name pioglitazone (r0, r2) • Sitagliptin (r0, r2) • Sitagliptin-metformin (r0, r2) • Saxagliptin (r0, r2) <p>Plans either fully restricted brand name pioglitazone, sitagliptin, and sitagliptin-metformin across the board or did not restrict any of the 3.</p>	<ol style="list-style-type: none"> 1. None of the 4 restricted 2. Saxagliptin (r2) 3. Brand name pioglitazone (r2), sitagliptin (r2), sitagliptin-metformin (r2), saxagliptin (r2)
Statins	<ul style="list-style-type: none"> • Generic atorvastatin • Generic lovastatin • Generic pravastatin • Generic simvastatin • Brand name atorvastatin • Ezetimibe-simvastatin^a • Rosuvastatin^a 	<ul style="list-style-type: none"> • Generic simvastatin (r0, r1) • Brand name atorvastatin (r0, r2) • Ezetimibe-simvastatin (r0, r1, r2) • Rosuvastatin (r0, r2) <p>Plans that partially restricted generic simvastatin also partially restricted ezetimibe-simvastatin.</p>	<ol style="list-style-type: none"> 1. None of the 4 restricted 2. Brand name atorvastatin (r2) 3. Ezetimibe-simvastatin (r2) 4. Generic simvastatin (r1), brand name atorvastatin (r2), ezetimibe-simvastatin (r1) 5. Brand name atorvastatin (r2), ezetimibe-simvastatin (r2) 6. Rosuvastatin (r2), ezetimibe-simvastatin (r2) 7. Rosuvastatin (r2), brand name atorvastatin (r2), ezetimibe-simvastatin (r2)
RAS Antagonists	<ul style="list-style-type: none"> • Generic benazepril • Generic enalapril • Generic lisinopril • Generic lisinopril-hydrochlorothiazide • Generic losartan • Generic losartan-hydrochlorothiazide • Generic quinapril • Generic ramipril • Generic amlodipine-benazepril • Olmesartan^a • Valsartan all^a • Valsartan-hydrochlorothiazide^a 	<ul style="list-style-type: none"> • Generic amlodipine-benazepril (r0, r2) • Olmesartan (r0, r2) • Valsartan (r0, r2) • Valsartan-hydrochlorothiazide (r0, r2) <p>Plans that fully restricted valsartan also fully restricted valsartan-hydrochlorothiazide.</p>	<ol style="list-style-type: none"> 1. None of the 4 restricted 2. Generic amlodipine-benazepril (r2) 3. Olmesartan (r2) 4. Generic amlodipine-benazepril (r2), olmesartan (r2) 5. Olmesartan (r2), valsartan (r2), valsartan-hydrochlorothiazide (r2)

OHA indicates oral hypoglycemic agent; r0, none restricted; r1, partially restricted; r2, all restricted; RAS, renin-angiotensin system antagonists.
^aSingle-source brand name drugs in 2012.

restrictions were mostly placed on brand name drugs, whereas almost all generic drugs were readily available on formulary. In addition, the benchmark PDPs appeared to have 3 formulary approaches for handling brand name drugs (Tables 2-4). From most restrictive to most generous, these directives were: 1) placing restrictions on all brand name drugs, 2) selectively covering brand name drugs without restrictions, and 3) covering all single-source brand name drugs and commonly used multi-source brand name drugs without restrictions.

The top panels in Tables 2-4 present descriptive statistics for annual days of supply for every drug that accounted for at least 1% of overall utilization in the LIS population, beginning with OHAs (Table 2), statins (Table 3), and RAS antagonists (Table 4). These statistics are displayed by the groups of formulary restrictions

described in Table 1. Placing formulary restrictions on a drug was associated with lower utilization of that medication, and the impact was more pronounced among statins and RAS antagonists than among OHAs.

Utilization of generic drugs was much higher among beneficiaries enrolled in plans that restricted access to brand name drugs. Compared with those enrolled in plans that placed no formulary restrictions on the 4 statins under study (Table 3), beneficiaries who faced restrictions in obtaining rosuvastatin (single-source brand name), atorvastatin (multi-source brand name), and ezetimibe-simvastatin (single-source brand name) not only had considerable fewer annual days of supply for the 3 drugs—rosuvastatin (9.10 for enrollees in plans with restrictions vs 35.41 for patients in plans with no restrictions), brand name atorvastatin (1.61 vs 20.52,

respectively), and ezetimibe-simvastatin (1.13 vs 7.99)—but they also had higher use of generic atorvastatin (58.99 vs 45.86), generic lovastatin (21.27 vs 16.66), generic pravastatin (48.72 vs 39.21), and generic simvastatin (136.30 vs 120.77). Similarly, beneficiaries who were subject to restrictions in accessing single-source brand name angiotensin II receptor blockers (ARBs), including olmesartan, valsartan, and valsartan-hydrochlorothiazide, had more days of supply for generic ARBs versus patients in plans not requiring plan approval (losartan: 50.18 vs 27.91, respectively; losartan-hydrochlorothiazide: 14.89 vs 8.57, respectively) (Table 4).

The bottom panels of Tables 2-4 present mean values for each of the study outcomes. The mean GDRs for the 3 OHA restriction groups varied from 0.83 for plans with no restrictions to 0.84 for plans restricting only saxagliptin (single-source brand name) and 0.88 for plans restricting brand name pioglitazone and single-source brand name dipeptidyl peptidase-4 (DPP-4) inhibitors (ie, saxagliptin, sitagliptin, and sitagliptin-metformin). The mean GDR for statins was also lowest for plans with no formulary restrictions (0.77), climbing to 0.95 for plans placing restrictions on brand name atorvastatin and single-source brand name statins (ie, rosuvastatin and ezetimibe-simvastatin). For RAS antagonists, plans with no restrictions again exhibited the lowest mean GDR (0.80), with the highest mean GDR (0.95) observed among plans restricting single-source brand name ARBs (eg, olmesartan, valsartan, and valsartan-hydrochlorothiazide). Mean costs per prescription fill were inversely related to GDR. The range for OHAs was \$54.54 in plans with the most restrictions to \$71.70 in plans with no formulary restrictions for the 4 OHAs under study. The range for statins was \$40.49 to \$73.04, respectively, and for RAS antagonists, \$20.78 to \$45.74, respectively. The differences in PDCs across plans by formulary restriction were small; in no instance was the difference greater than 0.04.

These relationships persisted after covariate adjustment for assignment year, beneficiary age, count of generics available for free via mail order, PDP region, and state law for generic substitution (Table 5). Regarding OHAs, restricting the use of brand name pioglitazone and single-source brand name DPP-4 inhibitors was associated with a GDR that was 3.0 percentage points higher (P

TABLE 2. Descriptive Statistics for Utilization of Individual Oral Hypoglycemic Agents and Study Outcomes Stratified by Formulary Restriction Policies^a

OHA Type	Group of Formulary Restrictions ^b			P ^c
	Brand Name Pioglitazone All, Sitagliptin All, Sitagliptin-Metformin All, Saxagliptin All (n = 6777)	Saxagliptin All (n = 11,530)	None of the 4 Restricted (n = 9775)	
Mean Annual Days of Supply				
Brand name pioglitazone	18.56	20.25	23.80	.5988
Sitagliptin ^d	25.25	35.61	38.80	.0263
Sitagliptin-metformin ^d	5.48	8.32	9.29	.1335
Saxagliptin ^c	6.55	4.22	4.72	.4374
Generic pioglitazone	7.61	7.81	9.17	.8854
Generic glimepiride	30.98	31.57	33.17	.4072
Generic glipizide	40.15	35.80	35.75	.3378
Generic glipizide XL	8.55	10.81	10.47	.6446
Generic glipizide ER	14.78	16.09	12.85	.2386
Generic glyburide	25.53	24.07	24.79	.8254
Generic glyburide-metformin	9.99	8.70	11.25	.3161
Generic metformin	188.77	184.74	181.13	.3244
Brand name drugs	55.83	68.39	76.60	.0474
Generic drugs	329.34	322.48	321.34	.3106
Study Outcomes				
Generic dispensing rate	0.88	0.84	0.83	.0018
Mean cost-per-prescription fill (\$)	54.54	65.77	71.70	.1607
Proportion of days covered	0.83	0.84	0.84	.3483

OHA indicates oral hypoglycemic agent.

^aN = 28,082.

^bDegree of restriction: "all" indicates all strengths restricted.

^cP values from type-3 tests. The P values in boldface font indicate that the differences between the groups are statistically significant.

^dSingle-source drugs in 2012.

<.0001) and a cost per prescription fill that was \$10.80 lower ($P = .0001$) for OHAs. Restricting access to brand name atorvastatin and single-source brand name statins was linked to a GDR that was 14.9 percentage points higher ($P < .0001$) and a cost per prescription fill that was \$29.60 lower ($P < .0001$) for statins. Restricting single-source brand name statins was associated with a cost per prescription fill that was \$25.60 lower ($P = .0158$), and restricting brand name atorvastatin and single-source brand name ezetimibe-simvastatin was related to a reduction of \$12.40 ($P = .0399$). Placing restrictions on single-source brand name ARBs was related to a GDR that was 15.0 percentage points higher ($P < .0001$) and a cost per prescription fill that was \$27.20 lower ($P < .0001$) for RAS

TABLE 3. Descriptive Statistics for Utilization of Individual Statins and Study Outcomes Stratified by Formulary Restriction Policies^a

Drug Type	Group of Formulary Restrictions ^b							P ^c
	Rosuvastatin All, Brand Name Atorvastatin All, Ezetimibe-Simvastatin All (n = 1810)	Generic Simvastatin Partially, Brand Name Atorvastatin All, Ezetimibe-Simvastatin Partially (n = 7939)	Brand Name Atorvastatin All, Ezetimibe-Simvastatin All (n = 22,104)	Rosuvastatin All, Ezetimibe-Simvastatin All (n = 5124)	Ezetimibe-Simvastatin All (n = 9525)	Brand Name Atorvastatin All (n = 13)	None of the 4 Restricted (n = 7349)	
Mean Annual Days of Supply								
Brand name atorvastatin	1.61	1.10	19.43 ^d	34.46	4.32	0.00	20.52	.1155
Ezetimibe-simvastatin ^d	1.13	8.32	0.71	0.33	0.42	0.00	7.99	<.0001
Rosuvastatin ^d	9.10	37.21	36.19	3.81	33.04	62.31	35.41	<.0001
Generic atorvastatin	58.99	64.04	42.40	27.44	54.23	36.92	45.86	.6105
Generic lovastatin	21.27	18.66	17.76	24.42	19.84	0.00	16.66	.1884
Generic pravastatin	48.72	35.29	35.64	36.91	41.92	34.62	39.21	.0822
Generic simvastatin	136.30	122.53	134.27	159.96	128.79	115.38	120.77	.0549
Brand name drugs	11.83	46.63	56.33	38.60	37.78	62.31	63.92	.0001
Generic drugs	265.48	240.85	230.21	248.73	244.94	186.92	223.02	.0198
Study Outcomes								
Generic dispensing rate	0.95	0.83	0.80	0.86	0.86	0.77	0.77	<.0001
Mean cost-per-prescription fill (\$)	40.49	68.66	60.48	41.44	53.05	59.29	73.04	<.0001
Proportion of days covered	0.81	0.83	0.83	0.83	0.82	0.80	0.83	.2406

^aN = 53,864.

^bDegree of restriction: "all" indicates all strengths restricted and "partially" indicates at least 1, but not all, strengths restricted.

^cP values from type 3 tests. Bolded P values indicate statistical significance.

^dSingle-source drugs in 2012.

antagonists. Restricting only olmesartan was linked to a GDR that was 3.8 percentage points higher ($P = .0434$) for RAS antagonists.

The estimated effects of formulary restrictions on overall adherence were minimal. Restricting access to brand name pioglitazone and single-source brand name DPP-4 inhibitors was linked to a PDC that was 0.4 percentage points higher ($P = .3508$), but the association was not statistically significant. Beneficiaries facing formulary restrictions of brand name atorvastatin and single-source brand name statins, on average, had a PDC that was 0.9 percentage points lower ($P = .1197$) compared with those that were not subject to such restrictions. Restricting the use of single-source brand name ARBs was related to a PDC that was 1.3 percentage points lower ($P = .0211$).

Stringent state laws for generic substitution (mandating generic substitution and only allowing brand name drugs by provider request) were associated with a GDR that was 3.3 percentage points higher for OHAs ($P = .0120$) and 3.0 percentage points higher for

RAS antagonists ($P = .0091$). Providing free mail order prescriptions for 1 additional generic statin was associated with a GDR that was 1.5 percentage points higher ($P = .0360$).

DISCUSSION

We found that placing formulary restrictions on brand name drugs generally shifted utilization away from brand name agents toward inexpensive generics. The effects were consistent across the 3 drug classes, but the magnitude of impact was smaller for OHAs than for statins or RAS antagonists. LIS recipients who faced restrictions in accessing brand name drugs had 34.9% (38.80 vs 25.25 days) fewer annual days of supply for sitagliptin than their counterparts who could freely access these drugs, 74.3% (34.41 vs 9.10 days, respectively) fewer days of supply for rosuvastatin, and 95.7% (28.06 vs 1.22 days, respectively) fewer days of supply

TABLE 4. Descriptive Statistics for Utilization of Individual Renin-Angiotensin System Antagonists and Study Outcomes Stratified by Formulary Restriction Policies^a

Drug Type	Group of Formulary Restrictions ^b					P ^c
	Olmesartan All, Valsartan All, Valsartan-Hydrochlorothiazide All (n = 1737)	Generic Amlodipine-Benazepril All, Olmesartan All (n = 765)	Olmesartan All (n = 28,595)	Generic Amlodipine-Benazepril All (n = 4831)	None of the 4 Restricted (n = 21,361)	
Mean Annual Days of Supply						
Generic amlodipine-benazepril	4.20	1.61	6.90	1.07	6.05	.0015
Olmesartan ^d	1.86	0.35	0.81	2.67	6.06	.0602
Valsartan ^d	1.22	24.10	24.61	27.03	28.06	.1330
Valsartan-hydrochlorothiazide ^d	0.55	13.87	10.42	11.40	14.25	.0107
Generic benazepril	5.38	23.15	13.36	12.49	11.35	.4324
Generic enalapril	24.71	14.65	18.18	17.53	16.25	.0068
Generic lisinopril	125.11	102.31	124.32	120.84	126.39	.5979
Generic lisinopril-hydrochlorothiazide	28.00	22.30	22.35	28.81	21.79	.8547
Generic losartan	50.18	22.24	32.44	26.15	27.91	.0142
Generic losartan-hydrochlorothiazide	14.89	8.90	10.02	11.30	8.57	.1046
Generic quinapril	2.99	6.56	3.36	4.26	3.49	.3798
Generic ramipril	11.11	5.66	6.04	8.50	6.89	.0006
Brand name drugs	3.64	38.31	35.83	41.09	48.38	.0607
Generic drugs	273.11	220.20	248.56	240.23	236.32	.0157
Study Outcomes						
Generic dispensing rate	0.95	0.81	0.85	0.82	0.80	.0304
Mean cost-per-prescription fill (\$)	20.78	41.01	38.89	43.31	45.74	.0610
Proportion of days covered	0.82	0.80	0.83	0.84	0.84	<.0001

^aN = 57,289.^bDegree of restriction: "all" indicates all strengths restricted.^cP values from type-3 tests.^dSingle-source drugs in 2012.

for valsartan (Tables 2-5). Correspondingly, the difference in GDR between the restricted and unrestricted groups was smaller for OHAs (0.88 vs 0.83, respectively) than for statins (0.95 vs 0.77) and RAS antagonists (0.95 vs 0.80).

This varying magnitude of impact might be due to differences in the availability of therapeutically equivalent agents. There were multiple generic statins and generic ARBs available in 2012, whereas all DPP-4 inhibitors were single-source brand name drugs. Clinical guidelines on diabetes management recommend adding a DPP-4 inhibitor, sulfonylurea, or thiazolidinedione (TZD) as a second oral agent for patients who cannot achieve their glycemic target with metformin monotherapy.¹⁵ We observed that beneficiaries who either did or did not face restrictions on DPP-4 inhibitors had comparable utilization of sulfonylureas and TZDs, indicating lack of substitution. Although the findings from the regression analysis suggested that restricting access to DPP-4 inhibitors has minimal impact on overall OHA adherence, further study is needed

to investigate concurrent adherence among patients treated with multiple OHAs and the clinical impact of formulary restrictions.

This study addressed the intended and unintended consequences of formulary restrictions, an understudied but important research topic given the near-ubiquity of these tools in modern formulary management.² The lack of literature is partially due to complexity in deciphering formulary designs, especially if a large number of drug products are involved. Most prior studies are limited to providing descriptive statistics regarding shares of restricted drugs or evaluating formulary policy changes for particular drugs.^{2,16,17} Our analysis of the benchmark for PDPs formularies contributed valuable insight in identifying meaningful formulary restrictions and understanding how they may influence medication utilization patterns. To the best of our knowledge, this is the first study that has systematically evaluated formulary restrictions and their impact on medication utilization and costs in the context of an entire drug class. It is a methodological advancement because utilization of

TABLE 5. Random Intercept Models—Estimated Effects of Formulary Restrictions on Study Outcomes^a

Formulary Model	Generic Dispensing Rate	Mean Cost-Per-Prescription Fill	Proportion of Days Covered
OHA Cohort (n = 28,082)			
Group of formulary restrictions (ref: none of the 4 restricted)			
Brand name pioglitazone all, ^b sitagliptin all, sitagliptin-metformin all, saxagliptin all	0.030 (0.005); <i>P</i> < .0001	-10.756 (2.812); <i>P</i> = .0001	-0.004 (0.005); <i>P</i> = .3508
Saxagliptin all	-0.004 (0.004); <i>P</i> = .3650	1.874 (2.423); <i>P</i> = .4393	0.002 (0.004); <i>P</i> = .6668
Count of generics with zero co-pay via mail order	-0.001 (0.001); <i>P</i> = .3780	0.008 (0.534); <i>P</i> = .9883	0.000 (0.001); <i>P</i> = .5899
State law for generic substitution (ref: allows generic substitution)			
Mandates generic substitution, allows brand name by patient request	-0.001 (0.000); <i>P</i> = .9320	-1.756 (2.904); <i>P</i> = .5455	0.011 (0.006); <i>P</i> = .0429
Mandates generic substitution, allows brand name by provider request	0.033 (0.013); <i>P</i> = .0120	-13.386 (5.111); <i>P</i> = .0088	0.014 (0.010); <i>P</i> = .1465
Statin Cohort (n = 53,864)			
Group of formulary restrictions (ref: none of the 4 restricted)			
Rosuvastatin all, brand name atorvastatin all, ezetimibe-simvastatin all	0.149 (0.029); <i>P</i> < .0001	-29.590 (6.802); <i>P</i> < .0001	-0.009 (0.006); <i>P</i> = .1197
Generic simvastatin partially, brand name atorvastatin all, ezetimibe-simvastatin partially	0.038 (0.030); <i>P</i> = .1997	-2.850 (7.057); <i>P</i> = .6863	-0.006 (0.004); <i>P</i> = .1353
Brand name atorvastatin all, ezetimibe-simvastatin all	0.002 (0.026); <i>P</i> = .9466	-12.401 (6.036); <i>P</i> = .0399	-0.005 (0.003); <i>P</i> = .0921
Rosuvastatin all, ezetimibe-simvastatin all	0.011 (0.045); <i>P</i> = .8143	-25.562 (10.589); <i>P</i> = .0158	-0.006 (0.005); <i>P</i> = .2395
Ezetimibe-simvastatin all	0.073 (0.027); <i>P</i> = .0068	-18.180 (6.378); <i>P</i> = .6648	-0.004 (0.003); <i>P</i> = .2265
Brand name atorvastatin all	-0.107 (0.102); <i>P</i> = .2953	11.275 (26.018); <i>P</i> = .2184	-0.033 (0.059); <i>P</i> = .5756
Count of generics with zero co-pay via mail order	0.015 (0.007); <i>P</i> = .0360	-2.044 (1.661); <i>P</i> = .2184	0.000 (0.001); <i>P</i> = .6988
State law for generic substitution (ref: allows generic substitution)			
Mandates generic substitution, allows brand name by patient request	-0.015 (0.006); <i>P</i> = .0207	0.184 (1.636); <i>P</i> = .9105	0.001 (0.004); <i>P</i> = .8935
Mandates generic substitution, allows brand name by provider request	0.002 (0.011); <i>P</i> = .8640	-4.882 (2.832); <i>P</i> = .0847	-0.003 (0.007); <i>P</i> = .6176
RAS Antagonist Cohort (n = 57,289)			
Group of formulary restrictions (ref: none of the 4 restricted)			
Olmesartan all, valsartan all, valsartan-hydrochlorothiazide all	0.150 (0.032); <i>P</i> < .0001	-27.216 (6.201); <i>P</i> < .0001	-0.013 (0.005); <i>P</i> = .0211
Generic amlodipine-benazepril all, olmesartan all	0.024 (0.027); <i>P</i> = .3894	-4.681 (5.431); <i>P</i> = .3888	-0.011 (0.008); <i>P</i> = .1670
Olmesartan all	0.038 (0.019); <i>P</i> = .0434	-3.220 (3.664); <i>P</i> = .3795	-0.004 (0.002); <i>P</i> = .0907
Generic amlodipine-benazepril all	0.008 (0.031); <i>P</i> = .8056	-1.185 (6.039); <i>P</i> = .8445	0.008 (0.004); <i>P</i> = .0357
Count of generics with zero co-pay via mail order	0.000 (0.003); <i>P</i> = .9916	-0.435 (0.572); <i>P</i> = .4468	0.001 (0.000); <i>P</i> = .0576
State law for generic substitution (ref: allows generic substitution)			
Mandates generic substitution, allows brand name by patient request	0.012 (0.006); <i>P</i> = .0500	-2.055 (1.308); <i>P</i> = .1162	0.003 (0.004); <i>P</i> = .3995
Mandates generic substitution, allows brand name by provider request	0.030 (0.012); <i>P</i> = .0091	-4.101 (2.374); <i>P</i> = .0841	0.002 (0.007); <i>P</i> = .7540

OHA indicates oral hypoglycemic agent; PDP, prescription drug plan; RAS, renin-angiotensin system; ref, reference.

^aAdjusted for assignment year, age, and PDP region. Each table cell presents a beta-coefficient (standard error) followed by *P* value.

^bDegree of restriction: "all" indicates all strengths restricted and "partial" indicates at least 1 but not all strengths restricted.

a drug is not only influenced by its own ease of access, but also formulary availability of other agents in the same therapeutic class.

The study estimates for the effects of formulary restrictions have high internal validity. By focusing on the randomized LIS recipients, we were able to minimize potential bias by isolating the effects of formulary restrictions from that of cost-sharing rules and removing confounding effects of virtually all beneficiary characteristics we could observe—and, by extension, other unobserved factors that represented critical threats to internal validity in conventional observational studies.

Additionally, LIS recipients represent about 40% of Part D enrollees, yet account for over 55% of total drug spending.¹⁸ This is a socially and economically disadvantaged population that often lives with disabilities and multiple chronic conditions. They tend to have worse health outcomes, yet significantly higher healthcare expenditures.⁹ Such disparities suggest the need to improve both quality and efficiency of care for this vulnerable population.

In 2012, full LIS recipients paid at most \$2.60 for generics and \$6.50 for brand name medications.⁸ We found that neither the availability of free generics via mail order nor generous coverage of brand name medications seemed to meaningfully affect LIS recipients' overall adherence to OHAs, statins, and RAS antagonists. Hence, LIS recipients' suboptimal adherence may be due to behavioral or clinical causes rather than costs or access issues.^{9,19} Part D plan sponsors and other healthcare decision makers may consider behavioral interventions to improve LIS recipients' perceived importance of medication adherence and disease management skills.

Limitations

This study has a few limitations. First, the study subjects were randomized to plans rather than varying formulary restrictions. Hence, the observed effects of formulary restrictions may be confounded by other plan-level policies that also affect medication utilization patterns. We observed that several benchmark PDPs provided free mail order prescriptions for commonly used generics, which would incentivize beneficiaries to take generics instead of brand name drugs and use more medications overall. We also observed that Envision RxPlus Silver did not offer 90-days-supply prescriptions in 2012, whereas all the other benchmark PDPs did. Conceptually, shorter length of drug supply per prescription fill presents more opportunities for filling prescriptions late and may lead to gaps in medication usage. To eliminate these 2 plan-level policies as alternative explanations for the observed effects of formulary restrictions on the study outcomes, we excluded beneficiaries enrolled in the Envision RxPlus Silver plan from all analyses and included a covariate for count of generics available for free via mail order in the regression models. In addition, we estimated random intercept regression models to recognize variability in unobserved plan attributes.

Second, our randomized cohorts of LIS beneficiaries were not strictly comparable from plan to plan within PDP regions.

Because Part D regional benchmark thresholds are determined annually through a competitive bidding process, plans can lose or gain benchmark status from year to year. When a plan loses benchmark status, its random assignees would be reassigned to other plans (however, there is an exception when the plan premium is just above the benchmark threshold). Additionally, the LIS recipients were randomized at different times. This dynamic randomization process resulted in small differences in beneficiary assignment year and age. To mitigate the potential confounding effects of beneficiaries' tenure in the plan and age, we included both assignment year and age as covariates in the regression analysis.

Readers should use caution in generalizing the findings of this study to non-LIS beneficiaries. Compared with non-LIS beneficiaries, LIS recipients tend to be younger, more socioeconomically disadvantaged, and more likely to live with disabilities and multiple chronic conditions. Nevertheless, both LIS and non-LIS beneficiaries in each plan faced the same formulary policies and appeal process for requesting coverage exceptions. Although the impact of formulary restrictions on the study endpoints may differ in magnitude, we expected the nature of the relationships to hold in non-LIS populations. Last, our study focused on existing users of OHAs, statins, and RAS antagonists. Future research may consider evaluating the impact of formulary noncoverage and UM tools on treatment initiation among individuals who are candidates for those chronic medications.

CONCLUSIONS

Placing formulary restrictions on brand name drugs shifts drug utilization toward generics and lowers cost per prescription fill, but has minimal impact on overall adherence for OHAs, statins, and RAS antagonists among Medicare Part D enrollees receiving LIS. ■

Author Affiliations: Department of Pharmaceutical Health Services Research (XS, BCS, SET, EMP), and The Peter Lamy Center on Drug Therapy and Aging (BCS), and Department of Epidemiology and Public Health (LSM), University of Maryland, Baltimore, MD; Information Products Group, Office of Information Products and Data Analytics, Center for Medicare and Medicaid Services (CAP), Baltimore, MD.

Source of Funding: This work was supported by a Young Investigator Adherence Award funded by the Pharmaceutical Research and Manufacturers of America (PhRMA) Foundation. The funder played no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Author Disclosures: The authors report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article. The views expressed in this paper are those of the authors and no official endorsement by HHS or CMS is intended or should be inferred.

Authorship Information: Concept and design (XS, LSM, EMP); acquisition of data (XS, BCS); analysis and interpretation of data (XS, LSM, EMP); drafting of the manuscript (XS, LSM); critical revision of the manuscript for important intellectual content (XS, BCS, CAP, SET, LSM, EMP); statistical analysis (XS, LSM); obtaining funding (XS); administrative, technical, or logistic support (CAP); and supervision (BCS, CAP, SET).

Address Correspondence to: Xian Shen, PhD, University of Maryland, Baltimore, 220 Arch St, Rm 12-328, Baltimore, MD 21201. E-mail: shenxian.1029@gmail.com.

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eAppendix

eAppendix Table 1. Formulary Restrictions on OHAs, Statins, and RAS Antagonists among Benchmark Plans*

Parent organization	Contract name	Formulary ID	Belongs to a national sponsor	Count of benchmark plans	Count of generics available for free via mail order	PIO	SIT	SIT-MET	SAX	ATO	SIM	ROS	EZT-SIM	AMD-BZP	OLM	VAL	VAL-HCT
Aetna Inc.	Aetna CVS/pharmacy Prescription Drug Plan	00012369	Y	26	None	0	0	0	2	0	0	0	0	0	0	0	0
Aetna Inc.	Aetna Medicare Rx Essentials	00012369	Y	1	None	0	0	0	2	0	0	0	0	0	0	0	0
CIGNA	BravoRx	00012359	Y	14	None	2	2	2	2	2	0	0	2	0	2	2	2
CIGNA	CIGNA Medicare Rx Plan One	00012331	Y	21	None	0	0	0	0	0	0	0	0	2	0	0	0
CIGNA	HealthSpring Prescription Drug Plan	00012352	Y	23	None	0	0	0	2	0	0	0	2	0	2	0	0
Coventry Health Care Inc.	First Health Part D Premier	00012336	Y	23	None	2	2	2	2	2	1	0	1	0	2	0	0
CVS Caremark Corporation	Community CCRx Basic	00012106	Y	30	None	0	0	0	2	2	0	0	2	0	0	0	0
CVS Caremark Corporation	Health Net Orange Option 1	00012050	N	17	None	0	0	0	0	2	1	0	1	0	0	0	0
CVS Caremark Corporation	CVS Caremark Value	00012289	Y	28	None	0	0	0	2	2	0	0	2	0	0	0	0
Express Scripts Holding Company	Medco Medicare Prescription Plan - Value	00012031	Y	16	None	0	0	0	0	0	0	0	2	0	2	0	0
Humana Inc.	Humana Walmart-Preferred Rx Plan	00012265	Y	34	OHA-6; STN-5; RAS-9	2	2	2	2	2	0	0	2	0	2	0	0
Munich	Windsor Rx	00012467	N	10	None	0	0	0	0	0	0	0	2	0	0	0	0

American Holding Corporation																	
Torchmark Corporation	First United American - Select	00012403	Y	1	OHA-3; STN-0; RAS-3	0	0	0	2	2	0	2	2	0	2	0	0
Torchmark Corporation	United American - Preferred	00012408	Y	1	OHA-3; STN-0; RAS-3	0	0	0	0	2	0	0	0	0	2	0	0
Torchmark Corporation	United American – Select	00012403	Y	19	OHA-3; STN-0; RAS-3	0	0	0	2	2	0	2	2	0	2	0	0
UnitedHealth Group, Inc.	AARP MedicareRx Preferred	00012261	Y	4	OHA-2; STN-2; RAS-4	0	0	0	0	0	0	0	0	0	0	0	0
WellCare Health Plans, Inc.	WellCare Classic	00012170	N	22	OHA-5; STN-4; RAS-8	0	0	0	0	0	0	2	2	0	2	0	0
WellPoint, Inc.	Blue MedicareRx Standard	00012353	Y	2	None	0	0	0	0	2	0	2	2	2	2	0	0
WellPoint, Inc.	MedicareRx Rewards Standard	00012353	Y	6	None	0	0	0	0	2	0	2	2	2	2	0	0

AMD-BZP indicates amlodipine-benazepril; ATO, brand-name atorvastatin; EZT-SIM, ezetimibe-simvastatin; MET, sitagliptin-metformin; OLM, olmesartan; PIO, brand-name pioglitazone; ROS, rosuvastatin; SIM, generic simvastatin; SIT, sitagliptin; SIT-SAX, saxagliptin; VAL, valsartan; VAL-HCT, valsartan-hydrochlorothiazide (0-none restricted, 1-partially restricted, 2-fully restricted)

eAppendix Table 2. Distribution of Study Subjects by PDP Region

PDP Region	Region Name	OHA Cohort, n=28,082		Statin Cohort, n=53,864		RAS Antagonist Cohort, n=57,289	
		#	%	#	%	#	%
1	Northern New England (New Hampshire ¹ and Maine ³)	89	0.32	223	0.41	192	0.34
2	Central New England (Connecticut ¹ , Massachusetts ³ , Rhode Island ² , and Vermont ²)	1482	5.28	3218	5.97	2865	5.00
3	New York ³	2251	8.02	4504	8.36	4421	7.72
4	New Jersey ²	543	1.93	1055	1.96	1095	1.91
5	Mid-Atlantic (Delaware ¹ , District of Columbia ¹ and Maryland ¹)	589	2.1	1154	2.14	1271	2.22
6	Pennsylvania ¹ , West Virginia ²	1100	3.92	2239	4.16	2196	3.83
7	Virginia ¹	661	2.35	1420	2.64	1473	2.57
8	North Carolina ¹	1322	4.71	2641	4.90	2869	5.01
9	South Carolina ¹	528	1.88	1176	2.18	1311	2.29
10	Georgia ¹	687	2.45	1372	2.55	1649	2.88
11	Florida ²	500	1.78	1055	1.96	1159	2.02
12	Alabama ¹ , Tennessee ²	1192	4.24	2236	4.15	2604	4.55
13	Michigan ¹	1245	4.43	2607	4.84	2593	4.53
14	Ohio ¹	1054	3.75	1992	3.70	2011	3.51
15	Indiana ¹ , Kentucky ²	1267	4.51	2578	4.79	2726	4.76
16	Wisconsin ¹	595	2.12	1220	2.26	1165	2.03
17	Illinois ¹	1389	4.95	2418	4.49	2570	4.49
18	Missouri ¹	343	1.22	672	1.25	746	1.30
19	Arkansas ¹	293	1.04	496	0.92	657	1.15
20	Mississippi ¹	796	2.83	1346	2.50	1702	2.97
21	Louisiana ¹	600	2.14	1078	2.00	1334	2.33
22	Texas ¹	1849	6.58	3147	5.84	3551	6.20
23	Oklahoma ¹	337	1.20	591	1.10	716	1.25
24	Kansas ¹	250	0.89	443	0.82	484	0.84
25	Upper Midwest and Northern Plains (Iowa ¹ , Minnesota ² , Montana ¹ , Nebraska ¹ , North Dakota ¹ , South Dakota ¹ and Wyoming ¹)	835	2.97	1840	3.42	1759	3.07
26	New Mexico ¹	167	0.59	232	0.43	288	0.50
27	Colorado ¹	180	0.64	301	0.56	348	0.61
28	Arizona ¹	204	0.73	270	0.50	372	0.65
29	Nevada ²	149	0.53	241	0.45	294	0.51

30	Oregon ¹ , Washington ²	776	2.76	1537	2.85	1556	2.72
31	Idaho ¹ , Utah ¹	168	0.60	288	0.53	315	0.55
32	California ¹	4548	16.2	8078	15.00	8756	15.28
33	Hawaii ²	40	0.14	77	0.14	85	0.15
34	Alaska ¹	53	0.19	119	0.22	156	0.27

State generic substitution law:

1. Allows for generic substitution by pharmacists if "brand only" not indicated by physician
2. Mandates generic substitution by pharmacists if "brand only" not indicated by physician and allows for brand if requested by patient
3. Mandates generic substitution by pharmacists if "brand only" not indicated by physician and only allows for brand if requested by prescriber

eAppendix Table 3. Characteristics of OHA Cohort by Parent Organization in PDP Region 3 (New York), n = 2251

Beneficiary Characteristics	Cigna, n=790	CVS Caremark, n=817	Express Script, n=363	Humana, n=87	Torchmark, n=**	UnitedHealth, n=84	WellCare, n=104	P
Assignment Year								<0.0001
2006	0, 0.0%	212, 26.0%	0, 0.0%	0, 0.0%	**	0, 0.0%	0, 0.0%	
2007	44, 5.6%	38, 4.7%	0, 0.0%	0, 0.0%	**	0, 0.0%	0, 0.0%	
2008	166, 21.0%	116, 14.2%	85, 23.4%	0, 0.0%	**	0, 0.0%	**	
2009	235, 29.8%	246, 30.1%	117, 32.2%	0, 0.0%	**	0, 0.0%	0, 0.0%	
2010	177, 22.4%	131, 16.0%	85, 23.4%	0, 0.0%	**	0, 0.0%	26, 25.0%	
2011	167, 21.1%	66, 8.1%	70, 19.3%	83, 95.4%	**	80, 95.2%	72, 69.2%	
2012	**	**	**	**	**	**	**	
Age	68.2	68.9	67.1	66.9	**	68.1	66.3	0.2079
Male	282, 35.7%	281, 34.4%	126, 34.7%	32, 36.8%	**	32, 38.1%	38, 36.5%	0.9744
Race								0.9109
White	400, 50.6%	415, 50.8%	176, 48.5%	40, 46.0%	**	44, 52.4%	53, 51.0%	
Black	171, 21.7%	188, 23.0%	82, 22.6%	22, 25.3%	**	11, 13.1%	26, 25.0%	
Hispanic	93, 11.8%	89, 10.9%	46, 12.7%	**	**	**	12, 11.5%	
Other	114, 14.4%	115, 14.1%	56, 15.4%	15, 17.2%	**	16, 19.1%	13, 12.5%	
Subsidy Level for Cost-Sharing								0.4684
Zero co-pay	169, 21.4%	161, 19.7%	81, 22.3%	19, 21.8%	**	**	19, 18.3%	
Low co-pay (\$1.1/\$3.3)	550,	586, 71.7%	257,	64,	**	66, 78.6%	73, 70.2%	

	69.6%		70.8%	73.6%				
High co-pay (\$2.6/\$6.5) or 15% coinsurance	71, 9.0%	70, 8.6%	25, 6.9%	**	**	**	12, 11.5%	
Old Age as Original Reason for Entitlement	431, 54.6%	460, 56.3%	191, 52.6%	49, 56.3%	**	50, 59.5%	52, 50.0%	0.6605
Diabetes	773, 97.9%	789, 96.6%	98.6%	87, 100.0%	**	83, 98.8%	102, 98.1%	0.1359
Hypertension	641, 81.1%	666, 81.5%	308, 84.9%	75, 86.2%	**	73, 86.9%	83, 79.8%	0.3867
Hyperlipidemia	553, 70.0%	586, 71.7%	248, 68.3%	68, 78.2%	**	60, 71.4%	72, 69.2%	0.5406
Chronic Kidney Disease	190, 24.1%	187, 22.9%	82, 22.6%	20, 23.0%	**	21, 25.0%	25, 24.0%	0.9884
Chronic Heart Failure	227, 28.7%	220, 26.9%	100, 27.6%	22, 25.3%	**	23, 27.4%	24, 23.1%	0.8531
Depression	189, 23.9%	211, 25.8%	94, 25.9%	21, 24.1%	**	21, 25.0%	27, 26.0%	0.9612
Charlson Comorbidity Index	1.7	1.5	1.7	1.7	**	1.5	1.7	0.2974
Count of Chronic Medications	8.7	8.9	9.0	8.8	**	8.8	8.5	0.8292
# of physician office visits	11.7	12.2	11.7	10.9	**	11.5	10.9	0.8146
# of Hospitalizations	0.5	0.5	0.5	0.6	**	0.4	0.5	0.8783
# of Emergency Room Visits	0.9	1.0	0.8	1.2	**	0.9	1.1	0.7330

**As per Internal Review Board requirement, we suppressed the statistics when $0 < n < 11$;

eAppendix Table 4. Characteristics of OHA Cohort by Parent Organization in PDP Region 22 (Texas), n = 1849

Beneficiary Characteristics	Aetna, n=295	Cigna, n=604	CVS Caremark, n=307	Coventry, n=268	Humana, n=81	Munich, n=**	Torchmark, n=**	WellCare, n=281	P
Assignment Year									<0.0001
2006	104, 35.3%	0, 0.0%	112, 36.5%	0, 0.0%	0, 0.0%	**	**	0, 0.0%	
2007	0, 0.0%	24, 4.0%	28, 9.1%	35, 13.1%	0, 0.0%	**	**	19, 6.8%	
2008	55, 18.6%	44, 7.3%	25, 8.1%	0, 0.0%	0, 0.0%	**	**	149, 53.0%	
2009	45, 15.3%	81, 13.4%	26, 8.5%	54, 20.2%	0, 0.0%	**	**	32, 11.4%	
2010	91, 30.9%	317, 52.5%	47, 15.3%	107, 39.9%	0, 0.0%	**	**	26, 9.3%	
2011	0, 0.0%	132, 21.9%	63, 20.5%	70, 26.1%	76, 93.8%	**	**	55, 19.6%	
2012	0, 0.0%	**	**	**	**	**	**	0, 0.0%	
Age	69.6	66.7	67.0	66.2	63.9	**	**	67.3	0.0023
Male	95, 32.2%	226, 37.4%	100, 32.6%	109, 40.7%	29, 35.8%	**	**	104, 37.0%	0.2536
Race									0.7882
White	173, 58.6%	333, 55.3%	161, 52.6%	148, 55.2%	44, 55.0%	**	**	151, 53.9%	
Black	40, 13.6%	90, 15.0%	47, 15.4%	46, 17.2%	14, 17.5%	**	**	39, 13.9%	
Hispanic	64, 21.7%	141, 23.4%	81, 26.5%	54, 20.2%	17, 21.3%	**	**	63, 22.5%	
Other	18, 6.1%	38, 6.3%	17, 5.6%	20, 7.5%	**	**	**	27, 9.6%	
Subsidy Level for Cost-Sharing									0.4713
Zero co-pay	39,	70,	41, 13.4%	35, 13.1%	**	**	**	32, 11.4%	

	13.2%	11.6%							
Low co-pay (\$1.1/\$3.3)	165, 55.9%	312, 51.7%	173, 56.4%	133, 49.6%	44, 54.3%	**	**	157, 55.9%	
High co-pay (\$2.6/\$6.5) or 15% coinsurance	91, 30.9%	222, 36.8%	93, 20.3%	100, 37.3%	31, 38.3%	**	**	92, 32.7%	
Old Age as Original Reason for Entitlement	170, 57.6%	360, 59.6%	157, 51.1%	153, 57.1%	48, 59.3%	**	**	146, 52.0%	0.1207
Diabetes	288, 97.6%	595, 98.5%	307, 100.0%	263, 98.1%	81, 100.0%	**	**	278, 98.9%	0.1232
Hypertension	250, 84.8%	522, 86.4%	270, 88.0%	231, 86.2%	67, 82.7%	**	**	234, 83.3%	0.5875
Hyperlipidemia	203, 68.8%	426, 70.5%	221, 72.0%	180, 67.2%	61, 75.3%	**	**	205, 73.0%	0.5671
Chronic Kidney Disease	87, 29.5%	145, 24.0%	88, 28.7%	72, 26.9%	27, 33.3%	**	**	67, 23.8%	0.2203
Chronic Heart Failure	77, 26.1%	147, 24.3%	77, 25.1%	68, 25.4%	19, 23.5%	**	**	83, 29.5%	0.6891
Depression	68, 23.1%	160, 26.5%	78, 25.4%	76, 28.4%	11, 13.6%	**	**	74, 26.3%	0.1276
Charlson Comorbidity Index	1.5	1.5	1.7	1.7	1.9	**	**	1.6	0.0599
Count of Chronic Medications	7.6	7.5	8.1	7.9	7.2	**	**	8.0	0.1226
# of physician office visits	10.3	9.5	9.7	9.9	10.0	**	**	10.0	0.8882
# of Hospitalizations	0.4	0.5	0.5	0.5	0.7	**	**	0.5	0.1410
# of Emergency Room Visits	1.2	1.2	1.3	1.5	1.6	**	**	1.4	0.6617

**As per Internal Review Board requirement, we suppressed the statistics when $0 < n < 11$;

eAppendix Table 5. Characteristics of OHA Cohort by Parent Organization in PDP Region 32 (California), n = 4548

Beneficiary Characteristics	CVS Caremark, n=1603	Humana, n=1094	WellCare, n=1851	P
Assignment Year				<0.001
2006	277, 17.3%	0, 0.0%	0, 0.0%	
2007	352, 22.0%	0, 0.0%	44, 2.4%	
2008	378, 23.6%	0, 0.0%	922, 49.8%	
2009	185, 11.5%	0, 0.0%	101, 5.5%	
2010	27, 1.7%	0, 0.0%	108, 5.8%	
2011	0, 0.0%	630, 57.6%	676, 36.5%	
2012	384, 24.0%	464, 42.4%	0, 0.0%	
Age	70.3	69.0	70.5	0.0023
Male	648, 40.4%	468, 42.8%	794, 42.9%	0.2842
Race				0.1238
White	761, 47.6%	497, 46.0%	805, 43.8%	
Black	120, 7.5%	103, 2.1%	170, 9.2%	
Hispanic	336, 21.0%	241, 22.3%	432, 23.5%	
Other	381, 23.8%	240, 22.2%	433, 23.5%	
Subsidy Level for Cost-Sharing				0.8107
Zero co-pay	132, 8.2%	93, 8.5%	170, 9.2%	
Low co-pay (\$1.1/\$3.3)	1,396, 87.1%	955, 87.3%	1,604, 86.7%	
High co-pay (\$2.6/\$6.5) or 15% coinsurance	75, 4.7%	46, 4.2%	77, 4.2%	
Old Age as Original Reason for Entitlement	964, 60.1%	645, 59.0%	1,095, 59.2%	0.7828
Diabetes	1,567, 97.8%	1,074, 98.2%	1,819, 98.3%	0.5229
Hypertension	1,302, 81.2%	867, 79.3%	1,519, 82.1%	0.1672
Hyperlipidemia	1,023, 63.8%	715, 65.4%	1,185, 64.0%	0.6853
Chronic Kidney Disease	431, 26.9%	274, 25.1%	527, 28.5%	0.1264
Chronic Heart Failure	377, 23.5%	250, 22.9%	428, 23.1%	0.9177
Depression	327, 20.4%	194, 17.7%	361, 19.5%	0.2253
Charlson Comorbidity Index	1.4	1.4	1.4	0.5773
Count of Chronic Medications	8.3	8.1	8.5	0.0152
# of physician office visits	9.8	9.9	10.0	0.8795
# of Hospitalizations	0.4	0.3	0.3	0.1628
# of Emergency Room Visits	0.9	0.9	1.0	0.5172

eAppendix Table 6. Characteristics of Statin Cohort by Parent Organization in PDP Region 3 (New York), n = 4504

Beneficiary Characteristics	Aetna, n=**	Cigna, n=1,608	CVS Caremark, n=1,631	Express Script, n=730	Humana, n=164	Torchmark, n=**	UnitedHealth, n=180	WellCare, n=182	P
Assignment Year									<0.0001
2006	**	0, 0.0%	398, 24.4%	0, 0.0%	0, 0.0%	**	0, 0.0%	0, 0.0%	
2007	**	101, 6.3%	66, 4.0%	0, 0.0%	0, 0.0%	**	0, 0.0%	**	
2008	**	338, 21.0%	256, 15.7%	182, 24.9%	0, 0.0%	**	0, 0.0%	**	
2009	**	462, 28.7%	516, 31.6%	225, 30.8%	0, 0.0%	**	0, 0.0%	0, 0.0%	
2010	**	355, 22.1%	260, 15.9%	165, 22.6%	0, 0.0%	**	0, 0.0%	50, 27.5%	
2011	**	348, 21.6%	126, 7.7%	150, 20.6%	157, 95.7%	**	177, 98.3%	122, 67.0%	
2012	**	**	**	**	**	**	**	**	
Age	**	68.5	69.8	68.8	65.7	**	67.8	65.9	<0.0001
Male	**	587, 36.5%	580, 35.6%	266, 36.4%	55, 33.5%	**	64, 35.6%	76, 41.8%	0.6477
Race									0.8169
White	**	894, 55.6%	896, 54.9%	416, 57.0%	93, 56.7%	**	91, 50.6%	97, 53.3%	
Black	**	294, 18.3%	315, 19.3%	124, 17.0%	27, 16.5%	**	33, 18.3%	45, 24.7%	
Hispanic	**	163, 10.1%	177, 10.9%	80, 11.0%	18, 11.0%	**	24, 13.3%	18, 9.9%	
Other	**	231, 14.4%	229, 14.0%	103, 14.1%	22, 13.4%	**	25, 13.9%	20, 11.0%	
Subsidy Level for Cost-Sharing									0.6950
Zero co-pay	**	337, 21.0%	331, 20.3%	152, 20.8%	31, 18.9%	**	30, 16.7%	34, 18.7%	
Low co-pay	**	1,110,	1,157,	516,	123,	**	134, 74.4%	133,	

(\$1.1/\$3.3)		69.0%	70.9%	70.7%	75.0%			73.1%	
High co-pay (\$2.6/\$6.5) or 15% coinsurance	**	161, 10.0%	143, 8.8%	62, 8.5%	**	**	16, 8.9%	15, 8.2%	
Old Age as Original Reason for Entitlement	**	874, 54.4%	915, 56.1%	393, 53.8%	87, 53.1%	**	104, 57.8%	95, 52.2%	0.7241
Diabetes	**	950, 59.1%	904, 55.4%	428, 58.6%	94, 57.3%	**	107, 59.4%	108, 59.3%	0.3696
Hypertension	**	1,263, 78.5%	1,282, 78.6%	598, 81.9%	123, 75.0%	**	147, 81.7%	131, 72.0%	0.0386
Hyperlipidemia	**	1,284, 79.9%	1,317, 80.8%	579, 79.3%	133, 81.1%	**	146, 81.1%	139, 76.4%	0.7669
Chronic Kidney Disease	**	367, 22.8%	361, 22.1%	156, 21.4%	34, 20.7%	**	43, 23.9%	45, 24.7%	0.8843
Chronic Heart Failure	**	435, 27.1%	439, 27.0%	206, 28.2%	39, 23.8%	**	48, 26.7%	45, 24.7%	0.8618
Depression	**	389, 24.2%	416, 25.5%	176, 24.1%	41, 25.0%	**	50, 27.8%	50, 27.5%	0.7878
Charlson Comorbidity Index	**	1.3	1.1	1.2	1.5	**	1.3	1.3	0.0107
Count of Chronic Medications	**	7.9	7.8	8.0	7.7	**	7.9	7.6	0.8494
# of physician office visits	**	11.3	11.6	11.2	10.8	**	11.7	10.7	0.8417
# of Hospitalizations	**	0.5	0.5	0.5	0.7	**	0.4	0.6	0.1576
# of Emergency Room Visits	**	0.8	0.8	0.8	1.1	**	0.7	0.9	0.6820

**As per Internal Review Board requirement, we suppressed the statistics when $0 < n < 11$;

eAppendix Table 7. Characteristics of Statin Cohort by Parent Organization in PDP Region 22 (Texas), n = 3147

Beneficiary Characteristics	Aetna, n=511	Cigna, n=1,053	CVS Caremark, n=552	Coventry, n=421	Humana, n=120	Munich, n=**	Torchmark, n=**	WellCare, n=476	P
Assignment Year									<0.0001
2006	189, 37.0%	0, 0.0%	208, 37.7%	0, 0.0%	0, 0.0%	**	**	0, 0.0%	
2007	**	47, 4.5%	47, 8.5%	62, 14.7%	0, 0.0%	**	**	26, 5.5%	
2008	91, 17.8%	87, 8.3%	43, 7.8%	0, 0%	0, 0.0%	**	**	258, 54.2%	
2009	80, 15.7%	161, 15.3%	43, 7.8%	77, 18.3%	0, 0.0%	**	**	53, 11.1%	
2010	150, 29.4%	498, 47.3%	93, 16.9%	174, 41.3%	0, 0.0%	**	**	51, 10.7%	
2011	0, 0.0%	246, 23.4%	110, 19.9%	101, 24.0%	110, 91.7%	**	**	87, 18.3%	
2012	0, 0.0%	14, 1.3%	**	**	**	**	**	**	
Age	70.0	66.7	68.3	67.0	65.6	**	**	68.9	<0.0001
Male	171, 33.5%	366, 34.8%	168, 30.4%	160, 38.0%	45, 37.5%	**	**	161, 33.8%	0.2158
Race									0.2538
White	293, 57.3%	602, 57.2%	327, 59.2%	244, 58.0%	58, 48.3%	**	**	259, 54.4%	
Black	77, 15.1%	174, 16.5%	88, 15.9%	72, 17.1%	30, 25.0%	**	**	73, 15.3%	
Hispanic	100, 19.6%	203, 19.3%	102, 18.5%	71, 16.9%	23, 19.2%	**	**	94, 19.8%	
Other	39, 7.6%	69, 6.6%	33, 6.0%	32, 7.6%	**	**	**	47, 9.9%	
Subsidy Level for Cost-Sharing									0.5592
Zero co-pay	74,	162,	90, 16.3%	63, 15.0%	16,	**	**	66, 13.9%	

	14.5%	15.4%			13.3%				
Low co-pay (\$1.1/\$3.3)	287, 56.2%	529, 50.2%	287, 52.0%	216, 51.3%	64, 53.3%	**	**	266, 55.9%	
High co-pay (\$2.6/\$6.5) or 15% coinsurance	150, 29.4%	362, 34.4%	175, 31.7%	142, 33.7%	40, 33.3%	**	**	144, 30.3%	
Old Age as Original Reason for Entitlement	310, 60.7%	577, 54.8%	308, 55.8%	240, 57.0%	73, 60.8%	**	**	269, 56.5%	0.3191
Diabetes	310, 60.7%	623, 59.2%	327, 59.2%	233, 55.3%	80, 66.7%	**	**	297, 62.4%	0.1829
Hypertension	432, 84.5%	878, 83.4%	464, 84.1%	354, 84.1%	102, 85.0%	**	**	405, 85.1%	0.9702
Hyperlipidemia	404, 79.1%	871, 82.7%	463, 83.9%	349, 82.9%	104, 86.7%	**	**	391, 82.1%	0.2661
Chronic Kidney Disease	147, 28.8%	275, 26.1%	150, 27.2%	98, 23.3%	34, 28.3%	**	**	124, 26.1%	0.5414
Chronic Heart Failure	144, 28.2%	308, 29.3%	143, 25.9%	107, 25.4%	32, 26.7%	**	**	152, 31.9%	0.2197
Depression	132, 25.8%	324, 30.8%	157, 28.4%	121, 28.7%	26, 21.7%	**	**	133, 27.9%	0.2005
Charlson Comorbidity Index	1.4	1.4	1.4	1.4	1.7	**	**	1.4	0.3832
Count of Chronic Medications	7.3	7.5	7.5	7.6	7.3	**	**	7.6	0.7716
# of physician office visits	9.3	9.9	9.5	9.6	8.7	**	**	9.7	0.6404
# of Hospitalizations	0.5	0.5	0.5	0.4	0.7	**	**	0.4	0.0557
# of Emergency Room Visits	1.0	1.3	1.3	1.5	2.2	**	**	1.2	0.0097

**As per Internal Review Board requirement, we suppressed the statistics when $0 < n < 11$;

eAppendix Table 8. Characteristics of Statin Cohort by Parent Organization in PDP Region 32 (California), n = 8078

Beneficiary Characteristics	CVS Caremark, n=2,895	Humana, n=1,939	WellCare, n=3,244	P
Assignment Year				<0.0001
2006	526, 18.2%	0, 0.0%	0, 0.0%	
2007	631, 21.8%	0, 0.0%	84, 2.6%	
2008	650, 22.5%	0, 0.0%	1,597, 49.2%	
2009	335, 11.6%	0, 0.0%	174, 5.4%	
2010	45, 1.6%	0, 0.0%	190, 5.9%	
2011	0, 0.0%	1,152, 59.4%	1,199, 37.0%	
2012	708, 24.5%	787, 40.6%	0, 0.0%	
Age	71.2	69.8	71.5	<0.0001
Male	1,166, 40.3%	828, 42.7%	1,332, 41.1%	0.2404
Race				0.2077
White	1,447, 50.0%	937, 48.3%	1,529, 47.1%	
Black	239, 8.3%	141, 7.3%	291, 9.0%	
Hispanic	463, 16.0%	322, 16.6%	548, 16.9%	
Other	734, 25.4%	515, 26.6%	859, 26.5%	
Subsidy Level for Cost-Sharing				0.4995
Zero co-pay	2877, 9.9%	191, 9.9%	316, 9.7%	
Low co-pay (\$1.1/\$3.3)	2,503, 86.5%	1,659, 85.6%	2,807, 86.5%	
High co-pay (\$2.6/\$6.5) or 15% coinsurance	105, 3.6%	89, 4.6%	121, 3.7%	
Old Age as Original Reason for Entitlement	1,777, 61.4%	1,173, 60.5%	2,016, 62.2%	0.4935
Diabetes	1,644, 56.8%	1,148, 59.2%	1,852, 57.1%	0.2088
Hypertension	2,313, 79.9%	1,549, 79.9%	2,617, 80.7%	0.6896
Hyperlipidemia	2,197, 75.9%	1,486, 76.6%	2,417, 74.5%	0.1898
Chronic Kidney Disease	730, 25.2%	461, 23.8%	848, 26.1%	0.1653
Chronic Heart Failure	722, 25.0%	464, 24.0%	832, 25.7%	0.3840
Depression	631, 21.8%	387, 20.0%	662, 20.4%	0.2367
Charlson Comorbidity Index	1.1	1.2	1.2	0.6396
Count of Chronic Medications	7.7	7.7	7.8	0.6024
# of physician office visits	10.0	9.6	9.7	0.3984
# of Hospitalizations	0.4	0.4	0.4	0.8407
# of Emergency Room Visits	0.9	1.0	0.9	0.5449

eAppendix Table 9. Characteristics of RAS Antagonist Cohort by Parent Organization in PDP Region 3 (New York), n = 4421

Beneficiary Characteristics	Aetna, n=**	Cigna, n=1,537	CVS Caremark, n=1,582	Express Script, n=755	Humana, n=153	Torchmark, n=**	UnitedHealth, n=184	WellCare, n=199	P
Assignment Year									<0.0001
2006	**	0, 0.0%	391, 24.7%	0, 0.0%	0, 0.0%	**	0, 0.0%	0, 0.0%	
2007	**	109, 7.1%	69, 4.4%	0, 0.0%	0, 0.0%	**	0, 0.0%	0, 0.0%	
2008	**	309, 20.1%	249, 15.7%	187, 24.8%	0, 0.0%	**	0, 0.0%	**	
2009	**	441, 28.7%	487, 30.8%	232, 30.8%	0, 0.0%	**	0, 0.0%	0, 0.0%	
20	**	323, 21.0%	253, 16.0%	171, 22.7%	0, 0.0%	**	0, 0.0%	63, 31.7%	
2011	**	351, 22.8%	125, 7.9%	154, 20.4%	146, 95.4%	**	177, 96.2%	124, 62.3%	
2012	**	**	**	11, 1.5%	**	**	**	**	
Age	**	69.4	70.4	69.9	66.2	**	67.7	65.0	<0.0001
Male	**	548, 35.7%	555, 35.1%	270, 15.8%	63, 41.2%	**	73, 39.7%	83, 41.7%	0.2761
Race									0.8318
White	**	796, 52.4%	797, 50.7%	388, 52.0%	78, 52.0%	**	83, 46.6%	103, 52.3%	
Black	**	332, 21.9%	362, 23.0%	163, 21.9%	35, 23.3%	**	46, 25.8%	53, 26.9%	
Hispanic	**	173, 11.4%	182, 11.6%	86, 11.5%	18, 12.0%	**	23, 12.9%	24, 12.2%	
Other	**	218, 14.4%	231, 14.7%	109, 14.6%	19, 12.7%	**	26, 14.6%	17, 8.6%	
Subsidy Level for Cost-Sharing									0.3876
Zero co-pay	**	304, 19.8%	298, 18.8%	152, 20.1%	26, 17.0%	**	33, 17.9%	31, 15.6%	

Low co-pay (\$1.1/\$3.3)	**	1,069, 69.6%	1,143, 72.3%	543, 71.9%	116, 75.8%	**	132, 71.7%	145, 72.9%	
High co-pay (\$2.6/\$6.5) or 15% coinsurance	**	164, 10.7%	141, 8.9%	60, 8.0%	11, 7.2%	**	19, 10.3%	23, 11.6%	
Old Age as Original Reason for Entitlement	**	892, 58.0%	933, 59.0%	437, 57.9%	82, 53.6%	**	107, 58.2%	99, 49.8%	0.1965
Diabetes	**	904, 58.8%	910, 57.5%	428, 56.7%	101, 66.0%	**	110, 59.8%	116, 58.3%	0.3835
Hypertension	**	1,347, 87.6%	1,408, 89.0%	681, 90.2%	134, 87.6%	**	165, 89.7%	163, 81.9%	0.0301
Hyperlipidemia	**	989, 64.4%	1,026, 64.9%	467, 61.9%	108, 70.6%	**	123, 66.9%	116, 58.3%	0.1352
Chronic Kidney Disease	**	338, 22.0%	351, 22.2%	162, 21.5%	34, 22.2%	**	50, 27.2%	48, 24.1%	0.6522
Chronic Heart Failure	**	442, 28.8%	463, 29.3%	205, 27.2%	42, 27.5%	**	55, 29.9%	56, 28.1%	0.9240
Depression	**	337, 21.9%	367, 23.2%	162, 21.5%	36, 23.5%	**	42, 22.8%	51, 25.6%	0.7899
Charlson Comorbidity Index	**	1.2	1.2	1.2	1.5	**	1.2	1.3	0.2105
Count of Chronic Medications	**	7.7	7.7	7.6	7.4	**	7.4	7.4	0.6328
# of physician office visits	**	11.1	11.9	10.5	9.7	**	10.8	9.5	0.0048
# of Hospitalizations	**	0.5	0.5	0.4	0.8	**	0.3	0.6	0.0034
# of Emergency Room Visits	**	0.8	0.9	0.7	1.1	**	0.8	1.1	0.2206

**As per Internal Review Board requirement, we suppressed the statistics when $0 < n < 11$;

eAppendix Table 10. Characteristics of RAS Antagonist Cohort by Parent Organization in PDP Region 22 (Texas), n = 3551

Beneficiary Characteristics	Aetna, n=537	Cigna, n=1,195	CVS Caremark, n=634	Coventry, n=502	Humana, n=129	Munich, n=**	Torchmark, n=**	WellCare, n=538	P
Assignment Year									<0.0001
2006	205, 38.2%	0, 0.0%	229, 36.1%	0, 0.0%	0, 0.0%	**	**	0, 0.0%	
2007	**	49, 4.1%	52, 8.2%	76, 15.1%	0, 0.0%	**	**	29, 5.4%	
2008	86, 16.0%	91, 7.6%	45, 7.1%	0, 0.0%	0, 0.0%	**	**	309, 57.4%	
2009	88, 16.4%	174, 14.6%	55, 8.7%	91, 18.1%	0, 0.0%	**	**	45, 8.4%	
2010	157, 29.2%	585, 49.0%	102, 16.1%	203, 40.4%	0, 0.0%	**	**	54, 10.0%	
2011	0, 0.0%	276, 23.1%	138, 21.8%	120, 23.9%	117, 90.7%	**	**	100, 18.6%	
2012	0, 0.0%	20, 1.7%	13, 2.1%	12, 2.4%	12, 9.3%	**	**	**	
Age	70.5	67.1	68.7	68.1	65.8	**	**	68.3	<0.0001
Male	178, 33.2%	441, 36.9%	209, 33.0%	196, 39.0%	44, 34.1%	**	**	187, 34.8%	0.2135
Race									0.0889
White	290, 54.3%	623, 52.4%	279, 55.8%	279, 55.8%	60, 47.2%	**	**	284, 53.1%	
Black	249, 20.9%	249, 20.9%	107, 21.4%	107, 21.4%	38, 29.9%	**	**	93, 17.4%	
Hispanic	239, 20.1%	239, 20.1%	126, 20.0%	80, 16.0%	24, 18.9%	**	**	120, 22.4%	
Other	79, 6.6%	30, 4.8%	30, 4.8%	34, 6.8%	**	**	**	38, 7.1%	
Subsidy Level for Cost-Sharing									0.0020
Zero co-pay	73,	144,	99, 15.6%	74, 14.7%	13,	**	**	59, 11.0%	

	13.6%	12.1%			10.1%				
Low co-pay (\$1.1/\$3.3)	308, 57.4%	597, 50.0%	327, 51.6%	239, 47.6%	66, 51.2%	**	**	304, 56.5%	
High co-pay (\$2.6/\$6.5) or 15% coinsurance	156, 29.1%	454, 38.0%	208, 32.8%	189, 37.7%	50, 38.8%	**	**	175, 32.5%	
Old Age as Original Reason for Entitlement	331, 61.6%	685, 57.3%	353, 55.7%	301, 60.0%	83, 64.3%	**	**	292, 54.3%	0.0625
Diabetes	332, 61.8%	694, 58.1%	374, 59.0%	273, 54.4%	81, 62.8%	**	**	307, 57.1%	0.1879
Hypertension	490, 91.3%	1,100, 92.1%	583, 92.0%	457, 91.0%	116, 89.9%	**	**	486, 90.3%	0.8308
Hyperlipidemia	340, 63.3%	757, 63.4%	412, 65.0%	321, 63.9%	94, 72.9%	**	**	345, 64.1%	0.4205
Chronic Kidney Disease	148, 27.6%	305, 25.5%	194, 30.6%	128, 25.5%	45, 34.9%	**	**	135, 25.1%	0.0474
Chronic Heart Failure	137, 25.5%	328, 27.5%	192, 30.3%	148, 29.5%	36, 27.9%	**	**	160, 29.7%	0.4643
Depression	129, 24.0%	314, 26.3%	162, 25.6%	140, 27.9%	34, 26.4%	**	**	144, 26.8%	0.8093
Charlson Comorbidity Index	1.3	1.3	1.5	1.5	1.8	**	**	1.3	0.0150
Count of Chronic Medications	7.1	6.9	7.1	7.1	7.3	**	**	7.0	0.8021
# of physician office visits	9.3	9.4	8.9	9.4	9.4	**	**	9.2	0.8804
# of Hospitalizations	0.4	0.5	0.6	0.5	0.8	**	**	0.5	0.0088
# of Emergency Room Visits	1.1	1.3	1.5	1.4	2.0	**	**	1.4	0.1125

**As per Internal Review Board requirement, we suppressed the statistics when $0 < n < 11$;

eAppendix Table 11. Characteristics of RAS Antagonist Cohort by Parent Organization in PDP Region 32 (California), n = 8756

Beneficiary Characteristics	CVS Caremark, n=3,090	Humana, n=2,078	WellCare, n=3,588	P
Assignment Year				<0.0001
2006	535, 17.3%	0, 0.0%	0, 0.0%	
2007	651, 21.1%	0, 0.0%	81, 2.3%	
2008	723, 23.4%	0, 0.0%	1,807, 50.4%	
2009	352, 11.4%	0, 0.0%	190, 5.3%	
2010	47, 1.5%	0, 0.0%	214, 6.0%	
2011	0, 0.0%	1,227, 59.1%	1,296, 36.1%	
2012	782, 25.3%	851, 41.0%	0, 0.0%	
Age	71.7	70.1	71.7	<0.0001
Male	1,205, 39.0%	1,206, 58.0%	2,117, 59.0%	0.0777
Race				0.9683
White	1,455, 47.3%	950, 46.2%	1,676, 47.0%	
Black	302, 9.8%	218, 10.6%	363, 10.2%	
Hispanic	567, 18.4%	381, 18.5%	668, 18.7%	
Other	751, 24.4%	509, 24.7%	861, 24.1%	
Subsidy Level for Cost-Sharing				0.8040
Zero co-pay	266, 8.6%	193, 9.3%	316, 8.8%	
Low co-pay (\$1.1/\$3.3)	2,689, 87.0%	1,786, 86.0%	3,119, 86.9%	
High co-pay (\$2.6/\$6.5) or 15% coinsurance	135, 4.4%	99, 4.8%	153, 4.3%	
Old Age as Original Reason for Entitlement	1,925, 62.3%	1,251, 60.2%	2,234, 62.3%	0.2350
Diabetes	1,787, 57.8%	1,202, 57.8%	2,030, 56.6%	0.5036
Hypertension	2,719, 88.0%	1,823, 87.7%	3,164, 88.2%	0.8789
Hyperlipidemia	1,838, 59.5%	1,249, 60.1%	2,137, 59.6%	0.8926
Chronic Kidney Disease	809, 26.2%	518, 24.9%	990, 27.6%	0.0824
Chronic Heart Failure	784, 25.4%	506, 24.4%	912, 25.4%	0.6301
Depression	634, 20.5%	400, 19.3%	692, 19.3%	0.3754
Charlson Comorbidity Index	1.1	1.1	1.2	0.6582
Count of Chronic Medications	7.4	7.3	7.5	0.3181
# of physician office visits	9.7	9.6	9.6	0.8915
# of Hospitalizations	0.4	0.4	0.4	0.7067
# of Emergency Room Visits	0.9	1.1	1.0	0.1234

eAppendix Figure. Selection of Study Cohorts

