ORIGINAL RESEARCH

Cost Sharing and Decreased Branded Oral Anti-Diabetic Medication Adherence Among Elderly Part D Medicare Beneficiaries

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BACKGROUND: Although the Medicare Part D coverage gap phase-out should reduce cost-related nonadherence (CRN) among seniors with diabetes, preferential generic prescribing may have already decreased CRN, while smaller numbers of patients using more costly branded oral anti-diabetic (OAD) medications remain vulnerable to CRN.

OBJECTIVE: To estimate the effects of cost sharing in the Part D standard (non-LIS) benefit on adherence to different OAD classes, comparing two classes dominated by inexpensive generic medications and two by more costly branded medications.

DESIGN AND PATIENTS: Retrospective cohort study using dispensed prescription data for elderly non-LIS ($N=81,047$) and LIS (low-income subsidy) ($N=150,359$) beneficiaries using same class OAD(s) in 2008 and 2009. Logistic regression modeled non-LIS likelihood; LIS and non-LIS patients matched using propensity outcome ($N=38,054$). Logistic regression, controlling for demographic and health status characteristics, modeled effects of non-LIS coverage on 2009 OAD class adherence.

MAIN MEASURES: Main outcome measures were within-class OAD coverage year adherence, with patients considered adherent when days supplied to calendar days ratio at least 0.8.

KEY RESULTS: Non-LIS patients had 0.52 and 0.57 times the odds of branded-only DPP-4 Inhibitor ($N=1,812$; 95 % CI: 0.43, 0.63; $P<0.001$) and Thiazolidinedione (TZD) ($N=6,290$; 95 % CI: 0.52, 0.63; $P<0.001$) adherence. Most patients ($N=32,510$; 82 %) used OADs in primarily generic classes, where we found no significant (Biguanides; $N=21,377$) or small differences (Sulfonylureas/Glinides [$N=19,240$; OR: 0.91; 95 % CI: 0.86, 0.97; $P=0.002$]) in adherence odds. Crude adherence rates were sub-optimal when CRN was not a factor (Non-LIS/LIS:

Biguanides: 65 %/65 %; Sulfonylureas/Glinides: 66 %/68 %; LIS: DPP-4 Inhibitors: 66 %; TZDs: 67 %).

CONCLUSIONS: Gap elimination would not affect generic, but should reduce branded OAD CRN. Branded copayments may continue to lead to CRN. Policy initiatives and benefit changes targeting both cost deterrents for patients with more complex disease and non-cost generic OAD underuse are recommended.

KEY WORDS: Medicare; medication adherence; diabetes; Part D; coverage gap.

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INTRODUCTION

The Medicare Part D coverage gap, which is to be eliminated in phases by 2020, has been controversial since this medication benefit was enacted with the 2003 Medicare Modernization Act. As a form of cost sharing, the gap could induce cost-related medication nonadherence (CRN), adversely affecting health status, particularly among individuals with chronic conditions.^{1–13} The introduction of the Part D program led to higher medication use rates among seniors, with recent studies indicating that other healthcare service use reductions partly offset program costs.^{14–28} Most Part D enrollees' expenditures do not reach the gap threshold: 12 % of enrollees, and 19 % of those who filled at least one prescription, reached the gap in 2009, lower proportions than in previous years.^{29,30} Still, enrollees who reach the gap are more likely to discontinue or reduce medication use.^{25,31–34} Closing the gap, scheduled and upheld with the Affordable Care Act, should decrease cost-related nonadherence.

Prescription drug market changes since the 2006 Medicare Part D program start, however, should also reduce CRN. Generic prescribing increases and patent protection

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expirations have led to lower medication prices and ongoing decreases in Part D beneficiaries' average daily medication costs.^{35–39} Understanding the effects of these changes on medication use is important for planning for the effects of gap elimination on medication adherence and program costs, and for targeted clinical and policy initiatives that improve adherence. To our knowledge, the effects of increasing generic product use on CRN among Part D enrollees have not been evaluated.

Generic medication availability and adherence are especially important for diabetes, where medication can prevent or delay the onset of complications and reduce hospitalization risks and costs.^{40–45} Diabetes is increasingly common among seniors, with prevalence rates estimated at 26.7 % and 390,000 cases diagnosed annually.⁴⁶ Generic medications are used as first-line and second-line therapies, with Metformin, a Biguanide, and Sulfonylureas (Glimepiride, Glipizide, Glyburide) available as inexpensive \$4 cash generics. Higher priced branded products like Januvia, with average 30-day prescription prices exceeding \$200, are recommended for more complex or advanced disease.^{47,48} In the Part D standard benefit, patients are responsible for 25 % copayments in the initial coverage phase, the full price at the gap, and the full price before meeting the standard deductible. These cost sharing components would not necessarily affect inexpensive generic oral anti-diabetic (OAD) adherence, but could deter branded OAD use. The gap phase-out should reduce more costly branded oral anti-diabetic CRN. The aim of this study was to evaluate the effects of cost sharing in the Part D standard benefit on adherence to different oral anti-diabetic medication classes.

METHODS

Study Design and Study Sample

Our evaluation was a retrospective cohort study of the effects of cost sharing in the Part D benefit on oral anti-diabetic adherence. Prescriptions filled in two OAD classes are mostly generic, while those in two others are exclusively branded. We hypothesized that Part D standard (non-LIS) coverage would adversely affect adherence in branded-only, but not primarily generic OAD classes. Because non-LIS patients could reduce more costly medication use throughout the coverage year, either in response to copayments and deductibles, or in order to delay or avoid the gap, we further hypothesized that CRN would be evident in coverage year branded OAD use rates. We compared non-LIS, whose coverage contained a gap, deductible and copayments, to low-income subsidy (LIS) beneficiaries, who faced no gap, no deductible, and minimal copayments. We built upon analyses conducted by IMS Health for the Kaiser Family Foundation that used IMS Health Longitudinal Prescription Database data to track medication spending and use among Part

D beneficiaries who filled prescriptions in specified therapeutic groupings, including oral anti-diabetics, at retail outlets in 2008 or 2009. Method of payment and health plan information were used to determine coverage type, and copayment to distinguish non-LIS from LIS enrollees.³⁰

We limited our study sample to patients ages 65 and older who filled OAD prescriptions at retail outlets where IMS had complete baseline (2008) and study (2009) year data. Study patients were limited to those who used OADs in the same class in the baseline and study years, because branded and generic medication prices were very different, and we were interested in CRN among patients able to anticipate coverage-year prescription expenses. We excluded non-LIS patients with coverage that could have provided medication benefits in the gap, such as Medicare Advantage or additional private coverage. Patients who started insulin or switched from one OAD class to another during the study year, who could appear nonadherent when they replaced an OAD with insulin or another OAD, were also excluded.⁴⁹ To address the possibility that patients died or entered nursing homes, for which we have no data, we required patients to have filled at least one prescription for any medication in the final quarter of the study year.⁵⁰ The final study sample comprised 231,406 patients who met all exclusion/inclusion criteria (Non-LIS: 81,047; LIS: 150,359), as shown in Figure 1.

Clinical experts identified and grouped oral anti-diabetic NDC codes into six classes, each with products not typically prescribed in combination: Biguanides; Sulfonylureas and Glinides; Combination Products; DPP-4 Inhibitors; Thiazolidinediones (TZDs); and Alpha-Glucosidase Inhibitors. Figure 2 shows the proportion of generic and branded OAD prescriptions filled in each class in 2009 across patients of all ages. Two classes, Biguanides and Sulfonylureas/Glinides, were dominated by generics, and included medications available as \$4 cash generics at retail outlets like Wal-Mart or Target. Two others, DPP-4 Inhibitors and TZDs, contained only branded prescription fills, with average 30-day prescription prices that exceeded \$200.⁴⁸ Our analyses focus on adherence in these four classes, which contained 90 % of all OAD fills in 2009, our study year.

We used prescription fill information to identify patient gender, age, baseline year risk score and comorbid medication use. Because the same medications can treat cardiovascular disease or hypertension, we assigned patients with at least one baseline year fill to a cardiovascular/hypertension comorbid group; other comorbidities were hyperlipidemia, reflected in at least one lipid-lowering medication fill, and mental health conditions. A Chronic Disease Score (CDS) variant, developed internally at IMS, was used to measure baseline year health status.⁵¹ CDS is a well-validated, pharmacy-based risk-adjustment tool that uses pharmacy fill data to identify patient

Figure 1. Cohort of diabetes patients.

Figure 2. Proportion of generic and branded prescriptions dispensed by oral anti-diabetic class.

risk in different patient populations.^{52–62} We refer to this measure as the risk score.

Because patients with more complex or advanced disease would be expected to use OADs in more classes, we developed a measure of diabetes complexity that was the number of unique oral anti-diabetic classes and insulin use in the baseline year.^{47,63} Because prescription fill data do not contain demographic information, we used retail pharmacy ZIP Code to develop an income proxy based on U.S. census ZIP Code median income. For geographic region, we mapped ZIP Code to one of four U.S. census regions. Our medication burden measure was the number of unique products for which patients had baseline year prescription fills. The time frames used to measure each variable are shown in Appendix A, available online.

Adherence Outcome

Our outcome measure was adherence within each oral anti-diabetic class. Because the Medicare Part D benefit is on a calendar year basis, we measured adherence over the study year (1/1/2009–12/31/2009). Since patients could have started the year with medication from 30-day, 60-day or 90-day supply prescriptions, we looked back to prescriptions filled in 2008 to identify medication on hand as of January 1, 2009. We calculated the days on which patients had medication available in each OAD class as the sum of days supplied for each fill over the calendar year, plus any days remaining from previous year fills, truncated at year-end. Prescriptions for different products within the same class were counted towards days supplied in that class.

Patients were considered adherent if the ratio of days supplied to calendar days was at least 0.8.^{64–66}

Statistical Analyses

To account for possible study sample selection issues, we developed a propensity score that modeled the likelihood of Part D non-LIS plan enrollment. We used logistic regression with “Non-LIS enrollment” (yes/no) as the outcome, and demographic and health status covariates as independent variables. Age was coded as deviations from the mean. Risk score, income and medication burden were grouped into deciles, with the lowest value the referent. Baseline year number of OAD classes, diabetes complexity, comorbid medication use, gender, region, and OAD use within each class (0/1) were additional independent variables; the South, with the largest number of patients, was the region referent, and Biguanides, with the most fills, the OAD class referent. To reduce covariate imbalance among non-LIS and LIS patients, we conducted one-to-one nearest-neighbor propensity-score matching via logistic regression to identify our final study sample.

We used logistic regression to model the likelihood of adherence within each oral anti-diabetic class, controlling for socio-demographic and health status variables. Non-LIS coverage was the primary independent variable. We used indicator variables for age, defined as 5-year age bands, with the largest grouping, 65–69, as referent. Other propensity model independent variables were included in the adherence models, except for OAD class use, which could be correlated with the adherence outcomes. The model was run using the propensity matched patient sample, with sensitivity analyses

conducted using the unmatched sample, and an analytic sample matched using less stringent criteria.¹

RESULTS

Patient Cohorts

Table 1 lists unmatched and matched analytic sample characteristics. Unmatched LIS were sicker (Risk score: 6.0 vs. 5.09), poorer (Income: \$40,308 vs. \$45,788), and differed from non-LIS on most characteristics, including insulin, comorbid medication use, and gender. Most (82 %) used primarily generic class OADs, with smaller proportions using TZDs (22 %) or DPP-4 Inhibitors (6 %). The 38,054 non-LIS and LIS patient sample, matched at five significant digits, was well-balanced in all observed characteristics, with differences in proportions one percentage point or less, and age (74.5 vs. 74.6), risk score (5.67 vs. 5.66), medication burden (21.9 vs. 21.7) and income (\$42,130 vs. \$42,330) means very close. Most (85 %) used Biguanides (56 %) and/or Sulfonylureas/Glinides (50 %, 51 %). Fewer (23 %) used branded-only TZDs (19 %) or DPP-4 Inhibitors (5 %), although most patients using branded-only OADs also used generics (62 %; 14 % of all). Compared to matched LIS patients, non-LIS crude adherence rates were identical for Biguanides (65 %), slightly lower for Sulfonylureas/Glinides (66 % vs. 68 %), and 13–14 percentage points lower for TZDs (54 % vs. 67 %) and DPP-4 Inhibitors (52 % vs. 66 %) (Fig. 3).

Effect of Coverage Gap on Adherence

In logistic regression, non-LIS patients had 0.52 times the odds of being adherent to DPP-4 Inhibitors (OR: 0.52; 95 % CI: 0.43, 0.63; $P < 0.001$) and 0.57 to TZDs (OR: 0.57; 95 % CI: 0.52, 0.63; $P < 0.001$). Non-LIS were less likely to be adherent to Sulfonylureas/Glinides (OR: 0.91; 95 % CI: 0.86, 0.97; $P = 0.002$), although the estimate was small. There were no statistically significant differences in Biguanide adherence odds. In logistic regressions using the unmatched sample and an analytic sample matched at four significant digits, the results were similar, with non-LIS patients having lower odds of DPP-4 Inhibitor (Unmatched: OR=0.56; 4-digit matched: OR=0.56; $P < 0.001$) and TZD (Unmatched: OR=0.63; 4-digit matched: OR=0.63; $P < 0.001$) adherence, no differences in Biguanide, and small differences in Sulfonylurea/Glinide (Unmatched: OR=0.92; Matched: OR=0.92; $P < 0.001$) adherence odds. Table 2 summarizes these results.

Additional Covariates

Mental health medication use was predictive of reduced Biguanide and Sulfonylurea/Glinide adherence likelihood, though the effects were small. Risk score was associated with reduced odds of adherence, with estimates for patients in the highest, relative to the lowest, decile ranging from 0.45 (DPP-4 Inhibitors; 95 % CI: 0.24, 0.85; $P = 0.04$) to 0.71 (Biguanides; 95 % CI: 0.60, 0.85; $P < 0.001$). Full model results are shown in Table 3. Appendices B, C, and D, available online, contain full model results for our sensitivity analyses.

DISCUSSION

Compared to propensity matched LIS, non-LIS patients had 0.52 and 0.57 times the odds of being adherent to DPP-4 Inhibitors and TZDs, respectively, oral anti-diabetic classes dominated by branded products with an average 30-day supply price in 2009 exceeding \$200,⁴⁸ results consistent with the unmatched sample. Under the Part D standard benefit, these patients would have faced \$50 or higher monthly copayments after fulfilling their deductible, and the full price, \$200 or more, at the coverage gap. LIS patients would have had minimal copayments for all medications. To the extent that patients prescribed branded oral anti-diabetics have more advanced or complex disease and increased complication risks, higher risk non-LIS patients face medication prices that make CRN more likely.

Almost all patients in our sample, however, used primarily generic class OADs, including approximately 70 % who used only Biguanides and/or Sulfonylureas/Glinides (Table 1). We found no statistically significant differences in Biguanide adherence odds, although non-LIS patients were less likely to be adherent to Sulfonylureas/Glinides. The 0.91 estimate, however, was small and, while not as commonly prescribed as the Sulfonylureas, costs for branded-only Prandin, the more popular Glinide, may affect adherence. Our findings that most non-LIS diabetes patients use inexpensive generic OADs, where Part D cost sharing components do not adversely affect adherence, are consistent with a recent analysis that found that the Part D benefit does not affect coverage year adherence to medications recommended for diabetes patients.⁶⁷ Our finding that smaller numbers of patients using more costly branded OADs are vulnerable to CRN, however, is consistent with studies that report medication use reductions at the gap, including an IMS/KFF analysis that found considerably higher branded, compared to generic, prescription reductions among patients who reached the gap (18 % vs. 3 %).³⁰

¹Our analytic sample contained patients matched at five significant digits. Sensitivity analyses were conducted using a sample of patients matched at four significant digits.

Table 1. Characteristics of Study Sample

	Unmatched sample		Matched sample	
	Non-LIS	LIS	Non-LIS	LIS
Patients (N, %)	81,047 (35 %)	150,359 (65 %)	19,027 (50 %)	19,027 (50 %)
Male (N, %)	37,672 (46 %)	46,271 (31 %)	12,412 (35 %)	12,430 (35 %)
Age (mean, SD)	74.5 (6.34)	74.5 (6.28)	74.6 (6.42)	74.5 (6.33)
Region (N, %)				
East	24,536 (30 %)	38,528 (26 %)	5,358 (28 %)	5,358 (28 %)
Midwest	18,739 (23 %)	20,796 (14 %)	2,924 (15 %)	2,964 (15 %)
South	27,997 (35 %)	60,685 (40 %)	8,017 (42 %)	7,856 (41 %)
West	9,775 (12 %)	30,352 (20 %)	2,742 (14 %)	2,849 (15 %)
Income (mean, SD)	\$45,788 (16,532)	\$40,308 (14,533)	\$42,330 (15,403)	\$42,130 (14,813)
Risk score (mean, SD)	5.09 (2.45)	6.0 (2.75)	5.66 (2.69)	5.67 (2.70)
Comorbid medication use (N, %)				
Hypertension/cardiovascular disease	73,571 (91 %)	141,348 (94 %)	17,943 (94 %)	17,957 (94 %)
Hyperlipidemia	64,778 (80 %)	121,415 (81 %)	15,766 (83 %)	15,757 (83 %)
Mental health	32,893 (41 %)	75,799 (50 %)	8,757 (46 %)	8,826 (46 %)
Medication burden (mean, SD)	19.1 (9.93)	24.3 (12.42)	21.7 (11.16)	21.9 (11.78)
OAD use (N, %)				
1 OAD	40,572 (50 %)	73,695 (49 %)	10,368 (54 %)	10,321 (54 %)
2 OADs	27,356 (34 %)	52,111 (35 %)	6,075 (32 %)	6,239 (33 %)
3+ OADs	13,119 (16 %)	24,553 (16 %)	2,584 (14 %)	2,467 (13 %)
Insulin use (N, %)	12,316 (15 %)	27,103 (18 %)	2,714 (14 %)	2,748 (16 %)
OAD use (N, %)				
Biguanides	44,416 (55 %)	79,837 (53 %)	10,671 (56 %)	10,706 (56 %)
Sulfonylureas/Glinides	39,957 (49 %)	76,546 (51 %)	9,549 (50 %)	9,691 (51 %)
TZDs	17,576 (22 %)	34,809 (23 %)	3,583 (19 %)	3,629 (19 %)
DPP-4 Inhibitors	5,147 (6 %)	9,266 (6 %)	946 (5 %)	866 (5 %)
Combination products	8,518 (11 %)	16,208 (11 %)	1,673 (9 %)	1,686 (9 %)
Alpha-Glucosidase Inhibitors	495 (0.6 %)	1,124 (0.7 %)	99 (0.5 %)	99 (0.5 %)
Generic and branded OAD use				
Any generic*	66,804 (82 %)	123,396 (82 %)	16,262 (85 %)	16,258 (85 %)
Only generic*	52,261 (64 %)	95,419 (63 %)	13,207 (69 %)	13,314 (70 %)
Any branded†	21,307 (26 %)	41,273 (27 %)	4,355 (23 %)	4,302 (23 %)
Branded and generic†	12,949 (16 %)	25,142 (17 %)	2,737 (14 %)	2,678 (14 %)

LIS low-income subsidy; OAD oral anti-diabetic; SD standard deviation; TZDs thiazolidinediones

*Biguanides and/or Sulfonylureas/Glinides; †DPP-4 Inhibitors and/or Glitazones

American College of Physicians guidelines recommend starting diabetes patients with Metformin, the most commonly prescribed Biguanide, adding or switching to other generic before branded products.⁴⁷ Our results suggest these guidelines are followed and, further, that generic prescrib-

ing has had a positive impact on oral anti-diabetic medication adherence. But diabetes patients taking branded OADs may be selective about which medications they use regularly, limiting higher-priced fills prior to and during the gap. In the short-term, with the gap phase-out providing

Figure 3. Use and crude adherence rates by oral anti-diabetic class.

Table 2. Estimates of Effects of Part D Standard (Non-LIS) Coverage on Adherence by Oral Anti-Diabetic Class

Oral anti-diabetic class	Part D standard (non-LIS) coverage
Propensity matched sample*	
Biguanides (N=21,377)	1.00 (0.95, 1.06), 1.00
Sulfonylureas / Glinides (N=19,240)	0.91 (0.86, 0.97), 0.002
TZDs (N=7,212)	0.57 (0.52, 0.63), < 0.001
DPP-4 Inhibitors (N=1,812)	0.52 (0.43, 0.63), < 0.001
Unmatched sample	
Biguanides (N=124,253)	1.000 (0.945, 1.058) 0.9954
Sulfonylureas/ Glinides (N=116,503)	0.921 (0.896, 0.947) < 0.001
TZDs (N=52,385)	0.629 (0.604, 0.655) < 0.001
DPP-4 Inhibitors (N=14,413)	0.559 (0.518, 0.603) < 0.001
Propensity matched sample #2†	
Biguanides (N=58,309)	1.008 (0.974, 1.043) 0.6424
Sulfonylureas / Glinides (N=53,968)	0.924 (0.891, 0.958) < 0.001
TZDs (N=23,533)	0.625 (0.592, 0.659) < 0.001
DPP-4 Inhibitors (N=6,563)	0.564 (0.510, 0.624) < 0.001

LIS low-income subsidy, TZDs thiazolidinediones

*Matched at five significant digits;

†Matched at four significant digits

50 % branded medication gap coverage, these patients may still limit branded OAD use when faced with gap copayments of \$100 or more. Initial coverage phase copayments may also constitute ongoing adherence deterrents, with the standard 25 % copayment, over \$50, considerably higher than generic OAD copayments. Patients whose benefit includes a deductible may also reduce use of branded OADs. Non-LIS beneficiaries' use of branded medications should be monitored as the Part D benefit structure changes

over the next several years, with evaluations of the effects of all Part D cost sharing components on more costly branded medication adherence recommended. Relaxing LIS entry criteria could improve adherence among non-LIS patients with limited financial means.

Finally, our estimates of non-LIS and LIS patients adherent to Biguanides and Sulfonylureas/Glinides, where cost sharing had a minimal effect on adherence, ranged from 65 % to 68 %, with similar proportions of LIS patients adherent to TZDs (67 %) and DPP-4 Inhibitors (66 %). These adherence rates in the absence of CRN are not optimal. Research into and interventions that target factors other than cost are recommended. Our finding that mental health medication use is predictive of lower adherence rates is of concern, as diabetes patients with depression have been found to have elevated cardiac risk and increased costs.⁵⁵ Initiatives targeting OAD adherence among patients with mental health issues are warranted.

Our study is subject to several limitations. The absence of mail order or institutional data could bias our results if non-LIS and LIS mail order use or hospitalization rates differed. Mail order represented less than 1 % of DPP-4 Inhibitor and TZD prescriptions in our study year, however,⁴⁸ and IMS/KFF evaluations indicate that the data on which our analyses are based are consistent with CMS medication usage estimates, and not adversely affected by missing prescription data.³⁰ Further, our nearly identical matched sample health status measures and similar Biguanide and Sulfonylurea crude adherence rates would be inconsistent with cohort hospitalization risk and rate differences. Our estimates that patients with the highest risk scores were less likely to be adherent,

Table 3. Estimates of Effects of Non-LIS Coverage and All Independent Variables on Adherence by OAD Class (Full Model Results)

	Odds ratio (95 % confidence interval), P value			
	Biguanides (N=21,377)	Sulfonylureas / Glinides (N=19,240)	TZDs (N=7,212)	DPP-4 Inhibitors (N=1,812)
Part D standard (non-LIS) coverage	1.00 (0.95, 1.06) 1.00	0.91 (0.86, 0.97) 0.002	0.57 (0.52, 0.63) < 0.0001	0.52 (0.43, 0.63) < 0.0001
Gender	0.95 (0.89, 1.01) 0.10	0.99 (0.93, 1.05) 0.69	1.02 (0.92, 1.13) 0.70	1.16 (0.94, 1.43) 0.18
Age group†				
70–74	1.06 (0.98, 1.13) 0.15	1.04 (0.95, 1.13) 0.41	1.12 (0.98, 1.27) 0.09	0.85 (0.65, 1.12) 0.24
75–79	0.99 (0.92, 1.08) 0.84	1.10 (1.00, 1.2) 0.04	1.03 (0.90, 1.19) 0.64	1.02 (0.76, 1.35) 0.92
80–84	0.95 (0.86, 1.05) 0.28	1.01 (0.92, 1.12) 0.79	1.15 (0.98, 1.35) 0.084	1.35 (0.976, 1.862) 0.07
85+	0.82 (0.73, 0.93) 0.002	1.04 (0.94, 1.16) 0.44	1.23 (1.01, 1.49) 0.043	1.17 (0.819, 1.67) 0.39
Region‡				
East	1.12 (1.04, 1.20) 0.003	1.08 (1.00, 1.16) 0.06	1.24 (1.10, 1.41) 0.0006	1.40 (1.10, 1.78) 0.006
Midwest	1.20 (1.10, 1.31) < 0.001	1.25 (1.14, 1.38) < 0.001	1.11 (0.96, 1.29) 0.17	0.71 (0.51, 0.97) 0.033
West	0.89 (0.81, 0.96) 0.005	0.87 (0.79, 0.97) 0.009	1.06 (0.92, 1.24) 0.41	0.88 (0.65, 1.18) 0.38
Risk§	0.97 (0.93, 1.00) 0.08	0.60 (0.49, 0.72) < 0.001	0.56 (0.42, 0.76) 0.001	0.45 (0.24, 0.84) 0.036
Comorbid Rx				
Mental health	1.07 (0.94, 1.21) 0.33	0.89 (0.83, 0.96) 0.002	0.97 (0.86, 1.08) 0.534	0.84 (0.67, 1.05) 0.13
CVD/anti-HTN	1.04 (0.954, 1.131) 0.38	1.05 (0.908, 1.216) 0.51	1.34 (1.09, 1.65) 0.006	0.86 (0.53, 1.37) 0.52
Lipid lowering	0.93 (0.863, 0.991) 0.03	1.10 (1.01, 1.20) 0.03	1.00 (0.86, 1.15) 0.96	0.83 (0.62, 1.11) 0.21
# of OAD classes used	0.97 (0.930, 1.007), 0.11	0.94 (0.90, 0.98) 0.004	0.96 (0.90, 1.02) 0.20	1.12 (0.97, 1.28) 0.11
Income§	0.86 (0.75, 0.98) 0.07	0.89 (0.76, 1.02) 0.11	0.87 (0.68, 1.11) 0.52	0.73 (0.46, 1.16) 0.61
Medication burden§	1.46 (1.22, 1.74) 0.0006	2.05 (1.68, 2.50) < 0.001	2.16 (1.58, 2.95) 0.002	1.86 (0.81, 4.3) 0.24

CVD cardiovascular disease, HTN hypertension, LIS low-income subsidy, OAD oral anti-diabetic

*Male=0; †relative to age group 65–69; ‡relative to South region; §highest vs. lowest decile

independent of coverage type, may reflect higher hospitalization rates among the sickest patients.

Our data contained only retail outlet prescription fills, potentially affecting our ability to control for differences between non-LIS and LIS patients. However, our sample size was large, and our matched samples similar on all observed characteristics. While approximately 75 % of non-LIS patients were eliminated in the matched sample, potentially limiting the generalizability of our results, sensitivity analyses using both the unmatched study sample and a propensity matched patient sample using less stringent matching criteria generated consistent results. However, propensity matching cannot control for unobserved variables, and it is possible that unobserved variables in the matched and unmatched analyses were responsible for our findings.

Thiazolidinedione clinical issues led to decreased use during our study year, 2009, potentially biasing our results if one cohort was more likely to stop using TZDs. We know of no evidence that non-LIS patients were more likely to stop TZDs because of clinical concerns. Our findings are generalizable to the effects of Part D cost sharing on adherence to more costly branded medications.

Finally, we measured adherence over the full study year, and our CRN estimates do not enable us to distinguish the effects of the coverage gap, deductible and copayments on branded OAD adherence. As the gap is phased out, other cost sharing components in the Part D benefit may continue to deter adherence to less widely used, more costly medications. Evaluation and monitoring of the impact of the gap phase-out on adherence to these medications prior to and at the coverage gap are recommended.

CONCLUSIONS

Research into and planning for eliminating the gap should account for the increasing use of inexpensive generic medications among Part D enrollees. Closing the gap may not affect medication use among seniors with medication regimens composed primarily of generic products, but should improve adherence for patients using branded medications with no generic alternatives. However, high copayments prior to and in the coverage gap may continue to adversely affect branded medication adherence. Benefit structure modifications that remove cost-related medication use deterrents are needed, as are initiatives that address non-cost factors in adherence to less expensive generic products.

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Conflict of Interest: Dr. Sacks was employed by IMS Health for the duration of this study. Drs. Burgess, Cabral, Pizer and McDonnell declare that they do not have a conflict of interest.

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