Prescription Drug Spending and Medication Adherence Among Medicare Beneficiaries with Heart Failure

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ABSTRACT

BACKGROUND: Evidence suggests that cost sharing adversely affects appropriate prescription drug use for chronic disorders. However, few studies have evaluated this effect in heart failure (HF), the most common cause of hospitalization in Medicare.

OBJECTIVE: To determine whether spending on HF pharmacotherapy by Medicare Part D enrollees was associated with prescription refill adherence.

METHODS: This correlational study used pooled data from the 2010-2012 Medicare Current Beneficiary Survey (MCBS). The analysis sample consisted of community-dwelling MCBS participants with self-reported HF and continuous Part D coverage during the year of participation. 3 drug classes were analyzed independently: beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARBs). 1,448 weighted participant-year records (derived from 964 individuals) met the inclusion criteria, of which 846 (58%) were included for beta-blockers, 633 (44%) for ACE inhibitors, and 229 (16%) for ARBs. Spending was measured by average out-of-pocket payment for the relevant prescription, standardized to a 30-day supply, as a percentage of average monthly income. Adherence was measured by the medication possession ratio (MPR): total days supplied for all but the last refill divided by number of days between the first and last fills of the year.

RESULTS: Accounting for sampling weights, the median (interquartile range) monthly income was \$1,472 (\$949-\$2,466), and average percentage of monthly income spent on a 30-day medication supply was 0.22% for beta-blockers, 0.19% for ACE inhibitors, and 0.90% for ARBs. Mean MPR was 88.9% for beta-blockers, 88.5% for ACE inhibitors, and 90.4% for ARBs. Risk-adjusted models showed that percentage of income spent on a beta-blocker prescription was directly associated with odds of nonadherence (MPR < 80%), odds ratio = 1.38, 95% CI = 1.01-1.89, $P = 0.045$, and inversely associated with beta-blocker MPR, $B = -4.17$, $SE = 1.23$, $P = 0.001$. No such association was observed for ACE inhibitors or ARBs.

CONCLUSIONS: Price sensitivity was evident for beta-blockers but not for antiangiotensin drugs, despite very low out-of-pocket costs and high adherence. This study is relevant to value-based pricing of HF management drugs in Part D plans.

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What this study adds

- This study of cost-sharing effects on adherence in heart failure focused on Medicare specifically and evaluated cost sharing using population survey data with matched claims.
- Out-of-pocket spending on beta-blockers (but not angiotensin antagonists) was significantly associated with a modest decline in adherence in a nationally representative sample of Part D enrollees with self-reported heart failure.
- Price sensitivity was evident for beta-blockers despite very low average out-of-pocket costs and high overall adherence.

Health insurers use cost-sharing strategies to discourage inappropriate use of prescription drugs, but this practice may reduce appropriate use as well. Studies have shown that patients with chronic diseases who have high medication cost-sharing requirements are less likely to fill the prescriptions they need to manage their illness.¹⁻¹⁰ Some evidence also links medication cost-sharing level to downstream health care use and costs.^{3,4,10-12} However, the effect of cost sharing on medication adherence has not been well characterized for patients with chronic heart failure (HF), which afflicts an estimated 6.5 million people in the United States.¹³

HF is the most common reason for hospital admission among Medicare beneficiaries and costs the United States over \$30 billion annually.^{14,15} Survival with HF depends on adherence to a burdensome daily regimen of multiple prescription drugs, dietary restrictions, and self-monitoring.¹⁶ Lack of adherence to pharmacotherapy may lead to worsening symptoms, hospitalizations, and poorer outcomes, whereas optimal adherence lowers the risks of hospitalization, emergency care, and death.¹⁶⁻¹⁸ Therefore, policies that may affect adherence warrant review. The objective of this study was to evaluate whether medication adherence was associated with cost sharing in prescription drug plans among Medicare beneficiaries with HF.

Methods

Sample Selection

A secondary analysis of pooled data from the 2010-2012 Medicare Current Beneficiary Survey (MCBS) Cost and Use files was conducted. The MCBS matches questionnaire responses to Medicare claims data in a representative sample of the national

What is already known about this subject

- Cost-sharing requirements in prescription drug plans deter at least some appropriate medication use in chronic disorders.
- Copays over \$10-\$20 adversely affected adherence to heart failure medications in age-diverse, commercially insured samples in 2 previous studies of claims data.

FIGURE 1 Sample Selection Procedure

ACE=angiotensin-converting enzyme; ARB=angiotensin II receptor blocker; MCBS=Medicare Current Beneficiary Survey.

Medicare population.^{19,20} The average response rate was 62.3%. Participants were included in this study if they replied “yes” on the survey when asked, “Has a doctor ever told you that you had congestive heart failure?” or “In the past 12 months, has a doctor told you that you had congestive heart failure?” (Figure 1). Use of Medicare claims to identify HF cases would have under-represented Medicare Advantage (MA) participants because claims for MA plans are unavailable in the MCBS.²¹ Using both claims and survey responses would have produced a sample without a clear target population, since MA participants would have been systematically missing in 1 segment of the sample (those with relevant claims but who did not self-identify).

Analysis was restricted to participants with Part D coverage in every month of the survey year, since only Medicare-covered prescriptions were analyzed; survey-reported prescriptions that did not match a Medicare record lacked the transaction data needed to calculate price and adherence.²² In addition, facility-dwelling participants were excluded because they may be given their medications directly by staff.² We focused on

3 classes of drugs commonly used in HF management: beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARBs). These agents are recommended for routine use in most patients with reduced ejection fraction (EF) and many with preserved EF, so infrequent refills were likely to reflect poor adherence rather than prescriber interruption.²³

Study Variables

MCBS does not report data on the cost-sharing requirements of Part D plans, but the files do contain payments for outpatient prescription drugs as documented in the Centers for Medicare & Medicaid Services Part D records.¹⁹ Out-of-pocket payments for the relevant drugs were taken from these records and standardized to a 30-day supply.^{3,9} The mean out-of-pocket payment was then computed for each drug and divided by the participant’s average monthly income, calculated from the annual income reported on the survey, which included Social Security, pension, and retirement account payments for the participant

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TABLE 1 Sample Characteristics and Population Estimates

Variable	n (Unweighted)	% (Weighted)	95% CI for % (Design-Adjusted) ^a	
Total	1,448	100.00	–	–
Sex				
Male	656	45.2	40.9	49.5
Female	792	54.8	50.5	59.1
Race				
Nonwhite ^b	326	22.9	18.9	27.0
White	1,120	77.1	73.0	81.1
Ethnicity				
Latino	113	8.5	5.8	11.1
Non-Latino	1,332	91.5	88.9	94.2
Marital status				
Married	572	41.9	37.8	46.0
Unmarried or widowed	875	58.1	54.0	62.2
Education				
No schooling	29	1.7	0.7	2.7
Nursery-8th grade	234	15.0	12.4	17.7
9th-12th grade	316	21.2	18.1	24.3
High school diploma	402	28.3	25.0	31.6
Vocational/technical, some college, or associate's degree	322	23.5	20.3	26.6
Bachelor's degree	88	6.9	4.9	8.9
Postgraduate	55	3.3	1.8	4.8
Census region				
Northeast/Midwest/West	744	52.8	48.1	57.4
South (includes PR)	704	47.2	42.6	51.9
Urbanicity				
Metro area	989	70.9	66.6	75.2
Nonmetro area	459	29.1	24.8	33.4
Medicare plan type				
Medicare Advantage	537	39.0	34.9	43.0
Traditional (FFS)	911	61.0	57.0	65.1
Health vs. others the same age				
Excellent	67	4.5	3.0	6.0
Very good	196	12.1	10.2	14.0
Good	425	28.7	25.8	31.6
Fair	467	33.3	30.4	36.3
Poor	284	21.3	18.6	24.1
Health now vs. 1 year ago				
Much better	83	6.0	4.6	7.4
Somewhat better	189	13.2	11.1	15.4
About the same	620	41.9	38.4	45.3
Somewhat worse	448	31.2	28.4	34.0
Much worse	104	7.7	5.9	9.5
Difficulty walking 2-3 blocks or a quarter of a mile				
None	265	19.1	16.2	22.0
A little	148	10.1	8.2	12.0
Some	167	11.8	10.0	13.6
A lot	251	17.6	15.4	19.8
Unable	609	41.4	37.8	44.9
Type 2 diabetes				
Yes	427	30.9	27.6	34.2
No	1,012	69.1	65.8	72.4
Smoking status				
Ever smoked	932	66.1	62.8	69.5
Never smoked	516	33.9	30.5	37.2

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TABLE 1 Sample Characteristics and Population Estimates (continued)

Variable		n (Unweighted)	% (Weighted)	95% CI for % (Design-Adjusted) ^a	
Medicare entitlement					
Disability or ESRD		273	23.5	19.6	27.4
Age only		1,174	76.5	72.6	80.4
Variable	Median (Weighted)	95% CI for Median (Design-Adjusted) ^a		Interquartile Range (Weighted)	
Age (years)	73.1	71.7	74.4	65.5	81.3
Annual income (thousands) ^c	17.7	16.1	19.3	11.4	29.6
Body mass index	28.7	28.1	29.2	24.7	33.0

^aReflects reliability of weighted population estimates, accounting for complex sampling design.

^bIncludes multiracial participants.

^cIncludes Social Security, retirement account, and pension payments for participant and spouse.

CI=confidence interval; ESRD=end-stage renal disease; FFS=fee-for-service; PR=Puerto Rico.

and the participant's spouse.¹⁹ The resulting proportion was multiplied by 100 to express out-of-pocket liability for each medication as a percentage of income.²¹

Adherence was estimated by the medication possession ratio (MPR), defined as the total days supplied for all but the last refill divided by the number of days between the first and last fills in each year, and expressed as a percentage.²⁴ Consistent with prior research, MPR values below 20% and above 120% were discarded, and MPR was dichotomized into <80% (non-adherent) and ≥80% (adherent) for categorical analysis.^{2,3,9} MPR was chosen over proportion of days covered to promote comparability with prior studies of copay effects on adherence in HF.^{3,9} Covariates included sex, race, Latino ethnicity, education, marital status, income, Census region, urbanicity, MA plan enrollment, age, self-rated health status (compared with others the same age and compared with 1 year before), body mass index (BMI), smoking status, self-reported type 2 diabetes, difficulty walking 2-3 blocks or a quarter of a mile, and basis for Medicare eligibility (disability or age).

Data Analysis

Associations between medication spending and MPR were tested separately for beta-blockers, ACE inhibitors, and ARBs. Participants who switched medications within the same drug class were excluded from the analysis of that class because left-over supply of the discontinued drug would have inflated the adherence estimate.^{3,7} Participants who filled the prescription only once during the year of observation were also excluded because at least 2 fills are necessary to compute the MPR.²⁴

Potential covariates were screened for associations with the MPR for each class. If an association with $P < 0.25$ was detected, then that covariate was included in the corresponding model.^{25,26} Design-adjusted logistic regression was used to model the effect of spending on dichotomized MPR, and design-adjusted multiple linear regression for the effect on absolute MPR value. The complex sampling design was addressed using sampling weights from MCBS and

Taylor-series linearization to estimate standard errors.^{26,27} For participants with multiple years of data, a weighted average of their cross-sectional sampling weights was applied because exclusion of multiyear participants in pooled analyses of MCBS data is not recommended.²⁸

A sensitivity analysis was conducted without recipients of the low-income subsidy (LIS) for Part D cost-sharing assistance because the LIS results in negligible out-of-pocket spending, which could have altered refill behavior.² Data were analyzed with SAS version 9.4 (SAS Institute, Cary, NC). The Emory University Institutional Review Board approved this study.

Results

Sample Characteristics

The final sample consisted of 1,448 participant-year records (derived from 964 unique beneficiaries). Of these, 846 (58%) were included in the beta-blocker analysis, 633 (44%) in the ACE inhibitor analysis, and 229 (16%) in the ARB analysis (Figure 1). Accounting for sampling weights, the sample was about 55% female, 23% nonwhite, and 8% Hispanic or Latino (Table 1). The weighted median age was 73 years. With respect to health status, 55% rated their health as fair or poor compared with others the same age, 39% said their health was worse than 1 year earlier, and 41% were unable to walk 2-3 blocks or a quarter of a mile. About 66% reported ever smoking tobacco, and 31% reported having type 2 diabetes. Based on BMI, nearly three quarters of participants were overweight or obese.

Out-of-pocket spending on the 3 drug classes analyzed was low: average amount spent, converted to a 30-day supply, was \$3.38 for beta-blockers, \$2.71 for ACE inhibitors, and \$15.49 for ARBs. In most cases, these amounts were well under 1% of the participant's average monthly income, the median of which was \$1,472. Estimated adherence was fairly high overall: mean MPR was 89% for beta-blockers, 88% for ACE inhibitors, and 90% for ARBs (Table 2). In bivariate analysis, the odds of nonadherence to beta-blockers were 26% higher and the MPR

TABLE 2 Unadjusted Estimates of Out-of-Pocket Costs and Adherence

Variable	Beta-Blockers			ACE Inhibitors			ARBs		
	Mean	95% CI		Mean	95% CI		Mean	95% CI	
Average OOP cost ^a as a % of monthly income	0.22	0.19-0.25		0.19	0.16-0.22		0.90	0.73-1.06	
MPR (%)	88.9	87.4-90.4		88.5	86.6-90.3		90.4	87.7-93.2	
Effect	Estimate	95% CI	P Value	Estimate	95% CI	P Value	Estimate	95% CI	P Value
Odds ratio for nonadherence ^b per unit change in OOP cost	1.26	0.94-1.70	0.12	0.86	0.48-1.53	0.61	0.91	0.64-1.27	0.57
Change in MPR per unit change in OOP cost	-3.55	–	0.01	-0.50	–	0.80	-0.18	–	0.88

Note: Estimates are weighted, and CIs and P values are adjusted for the complex sampling design.

^aStandardized to a 30-day supply.

^bMPR < 80%.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; CI = confidence interval; MPR = medication possession ratio; OOP = out of pocket.

was 3.6 percentage points lower per unit increase in share of income spent on the drug, but only the MPR result was statistically significant ($P=0.015$). The unadjusted results for ACE inhibitors and ARBs were ambiguous and not statistically significant (Table 2).

Multivariate Analysis

Logistic models of the adjusted odds of nonadherence to ACE inhibitors and ARBs (i.e., MPR < 80%) showed no significant effect from out-of-pocket spending on those drugs as a share of income (Table 3). On the other hand, the logistic model for beta-blockers showed that the adjusted odds of nonadherence were significantly associated with the share of income spent on that beta-blocker, odds ratio = 1.38, 95% confidence interval = 1.01-1.89, $P=0.045$. Similarly, the linear models for ACE inhibitors and ARBs showed no significant association between adherence and prescription drug spending as a share of income (Table 4). In the beta-blocker linear model, there was a significant inverse association between share of income spent on the beta-blocker and MPR, $B=4.17$, $SE=1.23$, $P=0.001$. Exclusion of the 45% of records for participants who received the LIS did not meaningfully alter the effect estimates (data not shown).

Discussion

Percentage of income spent on a beta-blocker prescription was associated with the odds of nonadherence and lower adherence estimates among Part D enrollees with HF. This finding corroborates an earlier study in a commercially insured HF sample that found significantly increased odds of nonadherence for beta-blocker copays over \$20.⁹ It must be interpreted with caution, however, because most participants spent far less than 1% of their monthly income on a beta-blocker prescription. Assuming a linear relationship, an increase of 0.1 in percentage of income spent (equivalent to moving from the 50th to 75th percentile in this sample) was associated with 4% increased odds of nonadherence. The same spending increase was associated with an average decline of 0.4 percentage points in MPR.

No association was found between out-of-pocket spending and adherence for ACE inhibitors or ARBs. It is unclear why this effect was observed for beta-blockers and not antihypertensive drugs. There may have been insufficient statistical power given the smaller sizes of the antihypertensive subsamples. In addition, MPR can slightly overestimate adherence by not adjusting for overlapping refills; assuming it was not systematically related to out-of-pocket price, any overestimate could have made price effects more difficult to detect. The only other published study of spending and adherence for ACE inhibitors in HF found that a \$10 rise in copay was significantly associated with decreased MPR, but that study was published 12 years ago.³ Most ACE inhibitors are now available off patent and appear on \$4 lists at major pharmacies. While average payments for beta-blockers and ACE inhibitors were similar in this sample, beta-blocker payments varied more widely, rising to a maximum of \$85.00 (compared with \$42.32 for ACE inhibitors).

One reason for the wide range of spending and adherence with beta-blockers may have been the greater use of brand-name products. Carvedilol was the agent used by 35% of the beta-blocker subsample. Generic carvedilol was not first labeled for chronic HF use until midway through the data collection period, and the controlled-release formulation is still brand name only.²⁹ Therefore, this agent may have been on higher-cost tiers in some Part D plans. In addition, beta-blockers are often prescribed after initiation of antihypertensive drugs, so patients may have already spent disposable income on ACE inhibitors or ARBs. With prevalent use of multiple drugs—71% of beta-blocker users also filled prescriptions for antihypertensive drugs—spending on other drug classes could have affected beta-blocker adherence. Nonetheless, a comparable number (73%) of antihypertensive users also filled a beta-blocker prescription, and over half of both groups filled prescriptions from 2 or more additional HF drug classes, so concomitant medication spending may not account for this difference in effect.

TABLE 3 Design-Adjusted Multiple Logistic Regression of Nonadherence (MPR<80%)

Effect	Beta-Blockers, n = 837		ACE Inhibitors, n = 632		ARBs, n = 225	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Percentage of monthly income ^a spent on 30-day supply	1.38 ^b	1.01-1.89	0.86	0.49-1.49	1.07	0.70-1.63
Age (years)	1.00	0.97-1.02	1.00	0.97-1.03	0.96	0.90-1.02
Income ^a (thousands)	–	–	0.99	0.98-1.00	0.99	0.96-1.02
Education	–	–	–	–	0.52 ^b	0.36-0.73
Health vs. others same age (5-point scale) ^c	–	–	–	–	1.22	0.84-1.79
Health now vs. 1 year ago (5-point scale) ^c	–	–	–	–	1.50	0.99-2.28
Race						
Nonwhite or multiracial	1.84 ^b	1.13-2.99	1.13	0.71-1.80	3.86 ^b	1.47-10.12
White	Reference		Reference		Reference	
Census region						
South (includes PR)	1.71 ^b	1.11-2.63	1.76 ^b	1.11-2.77	–	–
Northeast/Midwest/West	Reference		Reference			
Type 2 diabetes						
Yes	1.19	0.79-1.79	–	–	2.30	0.81-6.53
No	Reference				Reference	
Medicare entitlement						
Disability or ESRD	1.42	0.70-2.89	2.18 ^b	1.00-4.74	0.80	0.25-2.60
Age	Reference		Reference		Reference	
Medicare plan type						
Medicare Advantage	1.25	0.84-1.86	–	–	–	–
Traditional (FFS)	Reference					
Urbanicity						
Metro area	1.30	0.81-2.10	1.59	0.94-2.68	–	–
Nonmetro area	Reference		Reference			
Marital status						
Married	–	–	0.97	0.59-1.60	–	–
Unmarried or widowed			Reference			
Sex						
Male	–	–	–	–	2.58 ^b	1.08-6.20
Female					Reference	

Note: Sample sizes are unweighted counts of participant-year records and reflect listwise deletion of missing data.

^aIncludes Social Security, retirement account, and pension payments for participant and spouse.

^bSignificant at the $P < 0.05$ level.

^cHigher score indicates worse health.

ACE=angiotensin-converting enzyme; aOR=adjusted odds ratio; ARB=angiotensin II receptor blocker; CI=confidence interval; ESRD=end-stage renal disease; FFS=fee-for-service; MPR=medication possession ratio; PR=Puerto Rico.

The average out-of-pocket payment was nearly 5 times higher for ARBs than for beta-blockers, but the smaller ARB subsample could have made any effect between spending and adherence more difficult to detect. Also, ARBs are frequently prescribed when patients cannot tolerate ACE inhibitors; if patients have fewer options, they are less likely to be price sensitive even when the price is high. Indeed, mean MPR was highest for ARBs in this sample, indicating good adherence despite greater out-of-pocket costs. Furthermore, the patient and prescriber may discuss the relative prices of ARBs and ACE inhibitors in advance. If patients who cannot afford an ARB do not get a prescription in the first place, they would not appear in the Part D records. This form of self-selection may have affected the ARB analysis.

Side effects and dosing schedule offer possible noneconomic explanations. Common side effects of beta-blockers include erectile dysfunction, dizziness, and hyperglycemia, which could have interfered with adherence.³⁰ If these effects varied by out-of-pocket cost, then the models may have ignored an important source of confounding. ACE inhibitor side effects, on the other hand, are likely to prompt discontinuation and substitution with an ARB, which would not appear as nonadherence. It was not possible to assess side effects in this study. In addition, beta-blockers were likelier than ACE inhibitors to be dosed twice daily in a 2011-2012 chronic HF cohort, which could have contributed to the higher prevalence of nonadherence to beta-blockers in that study.³⁰ However, products with more frequent dosing may be on lower cost-sharing tiers,

TABLE 4 Design-Adjusted Multiple Linear Regression of MPR

Effect	Beta-Blockers, n = 805		ACE Inhibitors, n = 601		ARBs, n = 216	
	B	SE	B	SE	B	SE
Percentage of monthly income ^a spent on 30-day supply	-4.17 ^b	1.23	-0.93	1.82	-1.10	1.25
Age (years)	-0.02	0.08	-0.02	0.11	0.16	0.13
Income ^a (thousands)	-0.00	0.02	0.03	0.02	-0.00	0.03
Education	0.41	0.52	–	–	2.27 ^b	1.10
Health vs. others same age (5-point scale) ^c	-0.55	0.57	–	–	-2.02	1.19
Race						
Nonwhite or multiracial	-7.03 ^b	2.17	-3.33	2.18	-9.04 ^b	4.39
White	Reference		Reference		Reference	
Census region						
South (includes PR)	-4.05 ^b	1.45	-3.33	1.88	–	–
Northeast/Midwest/West	Reference		Reference			
Medicare entitlement						
Disability or ESRD	-3.83	2.82	-5.91	3.66	–	–
Age	Reference		Reference			
Benefit type						
Medicare Advantage	-2.57	1.69	–	–	–	–
Traditional (FFS)	Reference					
Ethnicity						
Latino	–	–	-7.63	4.50	–	–
Non-Latino			Reference			
Sex						
Male	–	–	–	–	-3.99	3.31
Female					Reference	

Note: Sample sizes are unweighted counts of participant-year records and reflect listwise deletion of missing data.

^aIncludes Social Security, retirement account, and pension payments for participant and spouse.

^bSignificant at the $P < 0.05$ level.

^cHigher score indicates worse health.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; B = unstandardized regression coefficient; ESRD = end-stage renal disease; FFS = fee-for-service; MPR = medication possession ratio; PR = Puerto Rico; SE = standard error.

which would have suppressed the association between cost and adherence rather than accounted for it.

Implications

To our knowledge, this is the first published study of medication cost sharing and adherence in HF to focus specifically on Medicare and the first to use population-level survey data. Since the MCBS is representative of Medicare beneficiaries nationally, our findings can be extrapolated to community-dwelling Medicare patients with self-reported HF and continuous Part D coverage. Moreover, this study demonstrates that analysis of MCBS data is a viable option for investigating cost sharing and adherence in the Medicare population generally.

If out-of-pocket spending indeed predicts nonadherence to beta-blockers in this population, then limits on patient liability for beta-blockers relative to income may increase efficiency, should costs rise. That is because adherence to HF treatment is associated with fewer hospitalizations,^{16,17} longer cardiac event-free survival,¹⁸ and lower cumulative Medicare

spending.²⁰ Moreover, copay-attributable nonadherence has been linked to increased risk of hospitalization in HF.³ In addition, the potential cost-effectiveness of full drug coverage has been demonstrated for medications in other cardiovascular disorders, especially postinfarction coronary heart disease.^{31,32} Similar economic analyses in the HF population are warranted.

Limitations

An important limitation of this study was its correlational design. Since prescription spending and adherence estimates were averaged over the survey year, nonadherent behavior could have occurred before observed out-of-pocket drug expenses. This problem of temporality limits any causal inference that can be made. Also, MPR estimates were not adjusted for observation time, so there was less opportunity to observe nonadherence in participants with shorter intervals between the first and last prescription fills, and MPR may have slightly overestimated adherence by not adjusting for overlapping fills.

Identification of HF cases with questionnaires may have missed respondents with incomplete awareness or understanding of their diagnosis. Selection bias may also have resulted from requiring at least 2 fills of the same agent to compute the MPR because this implies a minimum level of adherence.⁹ In addition, Part D enrollees may choose health plans with higher coverage of the drugs that they are already taking, which could have biased results toward the null hypothesis. Exclusion of participants who switched drugs within a class during the survey year could have obscured price-motivated nonuse, but again, including them would have overestimated adherence because of leftover supply of the discontinued drug.

No clinical data (e.g., EF) were available, so it was difficult to assess whether advancing illness made patients less price sensitive. The analysis did not include comorbidities other than type 2 diabetes because many relevant diagnoses were unavailable from the questionnaires and using claims would have required excluding MA enrollees. As already noted, the analysis also assumed that out-of-pocket spending on 1 drug class was independent of spending on another, yet there was substantial use of multiple drug classes.

Pooling data from multiple years could have underestimated standard errors because observations from participants who contributed data in multiple years were not independent. Nonetheless, when variance estimates account for cluster sampling, it may be unnecessary to correct for the additional autocorrelation from repeated observations.²⁸ Finally, we excluded survey-reported prescriptions that were not matched to Medicare records, but only about 6% of unmatched prescriptions for common chronic disease medications in the MCBS reflect true out-of-plan use for Part D participants; the rest are likely duplicates.²²

Conclusions

Despite having Part D drug coverage, some Medicare beneficiaries may have faced a modest financial barrier to optimal HF therapy: beta-blocker adherence was inversely related to out-of-pocket beta-blocker spending as a percentage of income in this study. Similar associations were not observed for ACE inhibitors or ARBs, possibly because of the sequence of prescribing or differences in side effects, dosing, or generic availability. Yet, the beta-blocker finding is notable because HF is a common cause of hospitalization, for which beta-blocker use reduces the risk. In addition, this finding has implications for newer products in HF management that carry higher out-of-pocket costs. Future research should use longitudinal data and address inpatient utilization to determine whether cost-sharing limits reduce poor outcomes in HF.

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REFERENCES

- Barron J, Wahl P, Fisher M, Plauschinat C. Effect of prescription copayments on adherence and treatment failure with oral antidiabetic medications. *P&T*. 2008;33(9):532-53.
- Chen SY, Shah SN, Lee YC, Boulanger L, Mardekian J, Kuznik A. Moving branded statins to lowest copay tier improves patient adherence. *J Manag Care Pharm*. 2014;20(1):34-42. Available at: <https://www.jmcp.org/doi/10.18553/jmcp.2014.20.1.34>.
- Cole JA, Norman H, Weatherby LB, Walker AM. Drug copayment and adherence in chronic heart failure: effect on cost and outcomes. *Pharmacotherapy*. 2006;26(8):1157-64.
- Colombi AM, Yu-Isenberg K, Priest J. The effects of health plan copayments on adherence to oral diabetes medication and health resource utilization. *J Occup Environ Med*. 2008;50(5):535-41.
- Doshi JA, Zhu J, Lee BY, Kimmel SE, Volpp KG. Impact of a prescription copayment increase on lipid-lowering medication adherence in veterans. *Circulation*. 2009;119(3):390-97.
- Henk HJ, Lopez JMS, Bookhart BK. Novel type 2 diabetes medication access and effect of patient cost sharing. *J Manag Care Spec Pharm*. 2018;24(9):847-55. Available at: <https://www.jmcp.org/doi/10.18553/jmcp.2018.24.9.847>.
- Kim YA, Rascati KL, Prasla K, Godley P, Goel N, Dunlop D. Retrospective evaluation of the impact of copayment increases for specialty medications on adherence and persistence in an integrated health maintenance organization system. *Clin Ther*. 2011;33(5):598-607.

8. Lee MJ, Khan MM, Salloum RG. Recent trends in cost-related medication nonadherence among cancer survivors in the United States. *J Manag Care Spec Pharm*. 2018;24(1):56-64. Available at: <https://www.jmcp.org/doi/10.18553/jmcp.2018.24.1.56>.
9. Patterson ME, Blalock SJ, Smith AJ, Murray MD. Associations between prescription copayment levels and beta-blocker medication adherence in commercially insured heart failure patients 50 years and older. *Clin Ther*. 2011;33(5):608-16.
10. Thornton Snider J, Seabury S, Lopez J, McKenzie S, Goldman DP. Impact of type 2 diabetes medication cost sharing on patient outcomes and health plan costs. *Am J Manag Care*. 2016;22(6):433-40.
11. Park H, Rascati KL, Lawson KA, Barner JC, Richards KM, Malone DC. Health costs and outcomes associated with Medicare Part D prescription drug cost-sharing in beneficiaries on dialysis. *J Manag Care Spec Pharm*. 2015;21(10):956-64. Available at: <https://www.jmcp.org/doi/10.18553/jmcp.2015.21.10.956>.
12. Subramanian S. Impact of Medicaid copayments on patients with cancer: lessons for Medicaid expansion under health reform. *Med Care*. 2011;49(9):842-47.
13. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics—2018 update: a report from the American Heart Association. *Circulation*. 2018;137(12):e67-e492.
14. Pfuntner A, Wier LM, Stocks C. Most frequent conditions in U.S. hospitals, 2011. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project statistical brief #162. September 2013. Available at: <https://www.hcup-us.ahrq.gov/reports/statbriefs/sb162.pdf>. Accessed April 9, 2019.
15. Heidenreich PA, Trogdon JG, Khavjou OA, et al. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation*. 2011;123(8):933-44.
16. Marti CN, Georgiopolou VV, Giamouzis G, et al. Patient-reported selective adherence to heart failure self-care recommendations, a prospective cohort study: the Atlanta Cardiomyopathy Consortium. *Congest Heart Fail*. 2013;19(1):16-24.
17. Esposito D, Bagchi AD, Verdier JM, Bencio DS, Kim MS. Medicaid beneficiaries with congestive heart failure: association of medication adherence with healthcare use and costs. *Am J Manag Care*. 2009;15(7):437-45.
18. Wu JR, Lennie TA, Dekker RL, Biddle MJ, Moser DK. Medication adherence, depressive symptoms, and cardiac event-free survival in patients with heart failure. *J Card Fail*. 2013;19(5):317-24.
19. Centers for Medicare & Medicaid Services. Medicare Current Beneficiary Survey: CY 2012 Cost and Use. 2016. Available at: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Research/MCBS/Codebooks-Items/2012CostAndUse.html?DLPage=2&DLEntries=10&DLSort=0&DLSortDir=descending>. Accessed May 8, 2019.
20. Lopert R, Shoemaker JS, Davidoff A, et al. Medication adherence and Medicare expenditure among beneficiaries with heart failure. *Am J Manag Care*. 2012;18(9):556-63.
21. Cubanski J, Neuman T, Damico A, Smith K. Medicare beneficiaries' out-of-pocket health care spending as a share of income now and projections for the future. Kaiser Family Foundation. January 26, 2018. Available at: <https://www.kff.org/medicare/report/medicare-beneficiaries-out-of-pocket-health-care-spending-as-a-share-of-income-now-and-projections-for-the-future/>. Accessed April 9, 2019.
22. Roberto PN, Stuart B. Out-of-plan medication in Medicare Part D. *Am J Manag Care*. 2014;20(9):743-48.
23. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128(16):1810-52.
24. Peterson AM, Nau DP, Cramer JA, Benner J, Gwadry-Sridhar F, Nichol M. A checklist for medication compliance and persistence studies using retrospective databases. *Value Health*. 2007;10(1):3-12.
25. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. *Source Code Biol Med*. 2008;3:17.
26. Heeringa SG, West BT, Berglund PA. *Applied Survey Data Analysis*. Boca Raton, FL: CRC Press; 2010.
27. Lewis TH. *Complex Survey Data Analysis with SAS*. Boca Raton, FL: CRC Press; 2017.
28. Briesacher BA, Tjia J, Doubeni CA, Chen Y, Rao SR. Methodological issues in using multiple years of the Medicare Current Beneficiary Survey. *Medicare Medicaid Res Rev*. 2012;2(1).
29. Raymond N. GSK wins \$235 million from Teva in Coreg patent trial. *Reuters*. June 21, 2017. Available at: <https://www.reuters.com/article/us-gsk-teva-pharm-ind-idUSKBN19C32B>. Accessed April 9, 2019.
30. Viana M, Laszczynska O, Mendes S, et al. Medication adherence to specific drug classes in chronic heart failure. *J Manag Care Pharm*. 2014;20(10):1018-26. Available at: <https://www.jmcp.org/doi/10.18553/jmcp.2014.20.10.1018>.
31. Choudhry NK, Patrick AR, Antman EM, Avorn J, Shrank WH. Cost-effectiveness of providing full drug coverage to increase medication adherence in post-myocardial infarction Medicare beneficiaries. *Circulation*. 2008;117(10):1261-68.
32. Ito K, Avorn J, Shrank WH, et al. Long-term cost-effectiveness of providing full coverage for preventive medications after myocardial infarction. *Circ Cardiovasc Qual Outcomes*. 2015;8(3):252-59.