Medicaid Beneficiaries With Congestive Heart Failure: Association of Medication Adherence With Healthcare Use and Costs

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Objectives: To examine the association of medication adherence with healthcare use and costs among Medicaid beneficiaries with congestive heart failure (CHF), to investigate whether the association was a graded one, and to estimate the potential savings due to improved adherence.

Study Design: Using Medicare and Medicaid data for 4 states, adherence was estimated using the medication possession ratio (MPR).

Methods: Multivariate logistic and 2-part general linear models were estimated to study the primary objectives. The MPR was specified in multiple ways to examine its association with healthcare use and costs.

Results: Adherent beneficiaries were less likely to have a hospitalization (0.4 percentage points), had fewer hospitalizations (13%), had in excess of 2 fewer inpatient days (25%), were less likely to have an emergency department (ED) visit (3%), and had fewer ED visits (10%) than nonadherent beneficiaries. Total healthcare costs were $5910 (23%) less per year for adherent beneficiaries compared with nonadherent beneficiaries. The relationship between medication adherence and healthcare costs was graded. For example, beneficiaries with adherence rates of 95% or higher had about 15% lower healthcare costs than those with adherence rates between 80% and less than 95% ($17,665 vs $20,747, $P < .01$). The relationship between adherence and total healthcare costs was even more stark when the most adherent beneficiaries were segmented into finer subgroups.

Conclusions: Healthcare costs among Medicaid beneficiaries with CHF would be lower if more patients were adherent to prescribed medication regimens. Researchers should reconsider whether a binary threshold for adherence is sufficient to examine the association of adherence with outcomes and healthcare costs.

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For author information and disclosures, see end of text.

Congestive heart failure (CHF) is a leading cause of hospitalization and mortality in the United States, affecting more than 5 million people at an expected cost of $34.8 billion in 2008.[1] The Centers for Medicare & Medicaid Services (CMS) has prioritized improved treatment of CHF, among other chronic conditions, through demonstrations and pilot programs for its beneficiaries.[2-4] The prevalence of CHF is as high as 2.6% among Medicaid beneficiaries and 10.7% among those dually enrolled in Medicare and Medicaid (dual eligibles).[5] Patients with CHF account for a disproportionate share of CMS spending. In 1999, 14% of fee-for-service Medicare beneficiaries with CHF accounted for 43% of total spending.[2]

Patients with CHF are generally at increased risk for heart attack, stroke, emergency department (ED) visits, hospitalization, and death.[6-8] To minimize their risk, most patients with CHF should use 1 or more drugs from different therapeutic subclasses, including loop diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, and β-blockers.[9-11] However, medication nonadherence is common among patients with CHF, and Medicaid beneficiaries' drug use is often inconsistent with practice guidelines.[12-17]

Despite evidence that poor adherence leads to higher hospitalization rates, few studies[18-20] have examined the relationship between adherence and healthcare costs for patients with CHF, although hospitalization accounts for their highest share of expenditures. If higher CHF drug adherence is associated with lower hospitalization risk, it stands to reason that it is also associated with lower healthcare costs.

This study had 3 primary objectives. The first objective was to examine the association of CHF medication adherence with healthcare use and costs in a Medicaid population. The second objective was to investigate whether the association between drug adherence and outcomes was a graded one. Throughout the literature, the primary threshold used to represent adherent behavior is a medication possession ratio (MPR) of 80%, but we hypothesized that the relationship was more likely graded. The third objective was to estimate the potential savings to Medicaid based on any findings that suggested an association between CHF medication adherence and healthcare costs.

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METHODS

Data and Sample Selection

This study used medical and phar-

Take-Away Points

Higher adherence to congestive heart failure (CHF) medications was associated with lower healthcare utilization and lower costs among Medicaid beneficiaries.

- The relationship between medication adherence and healthcare costs was a graded one. Beneficiaries with near-perfect drug adherence had lower healthcare costs than beneficiaries with only slightly lower adherence.
- Overall Medicare outlays could be considerably lower if more enrollees with CHF were adherent.
- Researchers should reconsider whether a simple binary threshold for adherence (eg, a medication possession ratio of 80%) is sufficient for examining the association of drug adherence with outcomes and healthcare costs.

macy claims data from the 1998 State Medicaid Research Files, the 1999 Medicaid Analytic eXtract, and the 1999 Medicare Standard Analytic File for Medicaid beneficiaries residing in Arkansas, California, Indiana, and New Jersey. We selected these states because they are geographically and demographically diverse and because they had limited or no capitated managed care for the disabled and older Medicaid population in 1998 and 1999. In addition, CHF drug utilization differences across these states were not due to differences in copayments or benefit designs.[17]

The research sample included noninstitutionalized beneficiaries with at least 1 CHF drug claim in 1999, medical claims for CHF, and continuous enrollment in fee-for-service Medicaid with pharmacy benefit coverage. The CHF medications were identified using First DataBank's Master Drug Data Base[21] therapeutic classification system and included the following drug groups: antianginals, β-blockers, calcium channel blockers, antiarrhythmics, antihypertensives, and diuretics. Beneficiaries were identified as having CHF if they were hospitalized with a CHF diagnosis in 1998 or had at least 2 ambulatory visits in 1998 with a CHF diagnosis (*International Classification of Diseases, Ninth Revision, Clinical Modification* codes 402.xx, 404.xx, and 428.x).

Medication Adherence

We used the MPR to measure CHF medication adherence in 1999.[22] Using all CHF drug claims, the MPR was calculated by dividing a patient's total days' supply of medication by the number of days between the date of the patient's first fill and the last day on which the patient had medication available. Days during which a patient stayed in a hospital are excluded from the calculation, and days for which more than 1 CHF drugs were available are counted only once. Using multiple CHF drug subclasses to examine adherence is more lenient than focusing on 1 subclass and is appropriate for a Medicaid population, as research indicates considerable underutilization of CHF drugs from any single subclass.[15,17]

This study considers multiple MPR specifications. First, the threshold of 80% is used to deem patients as adherent (≥80%) or as nonadherent (<80%). This value is borrowed from established literature on cardiovascular disease and from previous adherence research.[6,23-31] However, there is no clinical evidence to support using this ratio or any other value as the threshold for medication adherence. Second, in a sensitivity analysis we also specified the MPR as a continuous variable. Third, we specified the MPR as 4 different ordinal variables. The first ordinal variable has 3 levels, segmenting patients with an MPR of 95% or higher from patients with an MPR between 80% and less than 95% and from patients with an MPR below 80%. We also specified 3 different 5-level ordinal variables. First, we examined the MPR by adherence quintile (eg, the first quintile is 0%-20%, and the last quintile is 80%-100%). Second, we segmented the MPR by quintile such that roughly 20% of the sample fell into each group. Third, we specified an ordinal variable to examine adherence for patients with a near-perfect MPR (with each subgroup containing ≥10% of the sample). The 5 levels were 99% or higher, 95% to less than 99%, 80% to less than 95%, 50% to less than 80%, and less than 50%.

Outcome Variables and Regression Analyses

We examined healthcare costs and utilization in 1999. Cost outcomes included total healthcare (including and excluding drug costs) and drug, inpatient, outpatient, and other medical costs (skilled nursing facility, hospice, ED, and durable medical equipment). Utilization included any hospital use, the number of hospital admissions, the number of hospital days, any ED use, and the number of ED visits. Regression analyses examined the association in 1999 between CHF drug adherence and outcomes.

The distribution of costs dictated regression specifications for models in which costs were the dependent variables. For cost data with only nonzero values (total costs, including drug costs), we estimated a generalized linear model (GLM). For skewed data with many zero values, we used a 2-stage procedure.[32,33] We first estimated a logistic regression to model the likelihood of having a nonzero cost and then estimated costs with a GLM, multiplying cost estimates by the predicted probability of having nonzero costs to obtain final cost estimates. For all GLM equations, we used the modified Park test to determine the appropriate link function.[33] We estimated costs through the method of recycled predictions, setting all sample members as adherent or as nonadherent, while keeping all other individual characteristics constant.

Table 1. Study Population Characteristics and Congestive Heart Failure (CHF) Drug Use[a]

Variable	Total (N = 37,408)	Adherent to CHF Drug Regimens (n = 19,912)
Age, y, %		
≤64	35.9	34.5
65-74	24.4	26.1
75-84	24.7	25.4
≥85	15.1	14.0
Residence, %		
Arkansas	9.8	8.8
California	63.0	61.9
Indiana	8.9	9.8
New Jersey	18.3	19.5
Race/ethnicity, %		
African American	25.5	18.4
Other or unknown	20.9	32.0
White	53.6	49.7
Female sex, %	72.8	70.1
Dually enrolled in Medicare, %	72.0	69.9
Disabled, %	52.5	55.4
Had coronary artery disease, %	29.1	28.6
Had diabetes, %	29.8	28.6
Hospitalized for CHF in 1998, %	37.5	40.2
Hospitalized for other conditions in 1998, %	38.4	34.7
Chronic Illness and Disability Payment System risk score	1.07	0.98
No. of CHF prescriptions per month	1.2	1.7
No. of CHF drugs patients using, %[b]		
1	25.2	12.0
2-3	49.6	51.1
≥4	25.3	37.0
CHF medication possession ratio, %		
90-100	36.6	68.6
80-89	16.7	31.3
70-79	9.9	NA
0-69	36.9	NA

NA indicates not applicable.
[a]From the 1998 State Medicaid Research Files and the 1999 Medicaid Analytic eXtract. Beneficiaries are classified as adherent if their medication possession ratio is 80% or higher.
[b]Representing a drug subclass as defined by Master Drug Data Base, version 2, developed by Wolters Kluwer Health (http://www.medispan.com/master-drug-database.aspx).

For models in which adherence was specified as a 3-level or 5-level variable, we estimated costs for each of the 3 to 5 subgroups separately.

We estimated logit models for hospital admissions and ED visits and least squares regressions for the number of hospitalizations, the number of hospital days, and the number of ED visits. All utilization outcomes were estimated through recycled predictions. We estimated all regressions using commercially available statistical software (STATA, release 9; StataCorp LP, College Station, TX).[34]

Independent Variables

The independent variable of interest was the MPR. Regression analyses also included demographic characteristics,

Table 2. Regression-Adjusted Healthcare Utilization and Costs for Medicaid Beneficiaries Adherent and Nonadherent to Congestive Heart Failure Drug Regimens[a]

Variable	Adherent (n = 19,912)	Nonadherent (n = 17,496)	Difference[b]
Healthcare utilization			
Any hospitalization, %	47.5	47.9	–0.4
No. of hospitalizations	1.4	1.6	–0.2
No. of hospital days	5.9	8.0	–2.1
Any emergency department visit, %	43.7	45.1	–1.4
No. of emergency department visits	3.6	4.0	–0.4
Healthcare costs, $			
Total costs, including drug costs	19,402	25,312	–5910
Total costs, excluding drug costs	16,338	23,101	–6763
Drug costs	3516	2322	1194
Inpatient costs	7809	10,686	–2877
Outpatient costs	7766	9267	–1501
Other costs[c]	1313	1347	–34

[a]From the 1998 State Medicaid Research Files, the 1999 Medicaid Analytic eXtract, and the 1999 Medicare Standard Analytic File. Beneficiaries are classified as adherent if their medication possession ratio is 80% or higher.
[b]All significantly different from 0 at $P < .01$ (2-tailed t test) except for "Other costs" under "Healthcare costs."
[c]Include hospice, skilled nursing facility, home health, and emergency department.

health risk factors, and CHF comorbidities. Demographic characteristics included a dual-eligible indicator, age (≤64, 65-74, 75-84, and ≥85 years), sex, state of residence, and race/ethnicity (white, African American, or other). Health risk factors and comorbidities included whether the beneficiary also had diagnosed coronary artery disease or diabetes mellitus and whether the beneficiary had any hospitalizations related or unrelated to CHF during 1998, as well as a diagnostic risk adjustor based on the Chronic Illness and Disability Payment System[35] using 1998 medical claims data.

Potential Savings to Medicare

To estimate the potential savings to Medicare from higher CHF medication adherence, we extrapolated study findings on an aggregate level. This was based on published estimates of the number of beneficiaries with CHF and on assumptions about their mean medication adherence.[36]

RESULTS

In the 4 study states, 37,408 of Medicaid beneficiaries met the inclusion criteria (Table 1). About 36% were younger than 65 years, and 15% were 85 years or older. Slightly more than half were white, and roughly a quarter were African American. Almost three-fourths were female, 72% were dual eligibles, and about half were classified as disabled (and about half of these were also dual eligibles [data not shown]). Many beneficiaries had medical claims for other cardiovascular conditions in addition to CHF, including coronary artery disease (29%) and diabetes (30%). In 1998, 38% of the sample had a hospitalization for CHF, and 38% had a hospitalization for other conditions. In 1999, beneficiaries averaged 1.2 CHF drug claims per month. The most common CHF drug subclasses in the sample were diuretics (59% of patients), ACE inhibitors (45%), and antianginals (35%) (data not shown). Among adherent sample members as specified by an MPR threshold of 80%, the demographic profile was similar to that of the entire research sample, but the number of drug fills was higher.

Hospital and ED Use

Hospital and ED outcomes were always lower for adherent beneficiaries compared with nonadherent beneficiaries, and all differences were significant at $P = .01$ (Table 2). Adherent beneficiaries were less likely to have a hospitalization (0.4 percentage points), had fewer hospitalizations per beneficiary (13%), had in excess of 2 fewer days spent in the hospital (25%), were less likely to have an ED visit (3%), and had fewer ED visits per beneficiary (10%). When medication adherence was specified as an ordinal variable (at 3 or 5 levels), all healthcare utilization outcomes were generally least likely or lowest for beneficiaries with the highest MPR (data not shown).

Healthcare Costs

Except for total drug costs, healthcare costs were lower for adherent beneficiaries than for nonadherent beneficiaries ($P < .01$ for most comparisons) (Table 2). Total healthcare costs (including drug costs) were $5910 (23%) less per year. When the MPR was specified with 3 or more levels, the relationship between adherence and healthcare costs was graded (Table 3). For example, beneficiaries with adherence rates of 95% or higher had about 15% lower total healthcare costs, including drug costs, than those with adherence rates between 80% and less than 95% ($17,665 vs $20,747, $P < .01$). The same pattern was evident when the sample was split into quintiles by adherence level (20% intervals of the MPR) or by

Table 3. Regression-Adjusted Healthcare Costs for Medicaid Beneficiaries by Various Specifications of Medication Adherence[a]

Variable, %	Sample Size	Total Costs, $	Total Costs, Excluding Drug Costs, $	Inpatient Costs, $	Outpatient Costs, $
3 Level					
≥95	8527	17,665	14,418	7094	7196
80 to <95	11,385	20,747[b]	17,832[b]	8335[b]	8189[b]
<80	17,496	25,324[b]	23,112[b]	10,693[b]	9274[b]
5 Level					
≥99	3878	16,989	13,691	7084	6449
95 to <99	4649	18,141[b]	14,733[b]	7093	7776[b]
80 to <95	11,385	20,730[b]	17,675[b]	8332[b]	8180[b]
50 to <80	8989	24,350[b]	21,768[b]	10,424[b]	8231[b]
<50	8507	26,486[b]	24,349[b]	11,033[b]	10,414[b]

[a]From the 1998 State Medicaid Research Files, the 1999 Medicaid Analytic eXtract, and the 1999 Medicare Standard Analytic File. For regression specifications in which the medication possession ratio was split into quintiles, annual healthcare costs were always lowest for the quintiles with the highest adherence rates.
[b]Significantly higher than costs for the group with the highest adherence rates at $P < .01$ (2-tailed t test).

sample size (20% of the sample in each quintile). A specification by decile was also used, but the data are not shown.

The relationship between medication adherence rates and total healthcare costs was stronger when the most adherent beneficiaries were segmented into finer subgroups (Table 3). Beneficiaries with adherence rates of 99% or higher (near-perfect adherence) had 6% lower total healthcare costs, including drug costs, than patients with adherence rates between 95% and less than 99% ($16,989 vs $18,141, $P < .01$). The association of CHF medication adherence with costs was higher in absolute US dollars for dual-eligible beneficiaries adherent patients had annual costs (Table 4). Among dual-eligible beneficiaries, adherent patients had annual costs (including drug costs) that were $7913 lower than annual costs of nonadherent patients, or 24% of the nonadherent mean ($P < .01$). However, the difference between adherent and nonadherent beneficiaries among non–dual-eligible beneficiaries was only $2859 or 19% of the nonadherent mean ($P < .01$).

Potential Savings to Medicare From Improved Adherence

In 2002, approximately 13% of community-dwelling Medicare beneficiaries had CHF, and their mean healthcare costs were about $24,000.[36] Because more than 90% of Medicare enrollees reside in the community and the total number of enrollees in 2002 was about 40 million, roughly 5 million community-dwelling beneficiaries had CHF. Based on the association between medication adherence and healthcare costs for dual-eligible beneficiaries in this study, we estimated total costs to Medicare assuming that a fixed proportion of enrollees were adherent (≥80% MPR).

Because the mean annual healthcare costs for nonadherent dual eligibles were 23% higher than those for adherent dual eligibles, we estimated that the mean annual healthcare costs among nonadherent beneficiaries were $28,374 compared with $21,750 for adherent beneficiaries. If 60% of enrollees with CHF were adherent and that percentage rose to 80%, Medicare costs would be $6.6 billion lower, or about 2% of total Medicare spending. This estimate is sensitive to the initial proportion of beneficiaries who are presumed to be adherent. If 65% are adherent, then savings are about $5 billion. Moreover, these savings assume that Medicare could achieve higher mean patient adherence at little or no cost. However, because we had only 1 year of data, it is impossible to estimate the effect of persistent medication adherence from one year to the next.

Sensitivity Analyses

We conducted sensitivity analyses by specific drug subclass and by the number of distinct subclasses filled by beneficiaries. First, we specified the MPR as a continuous variable and estimated costs at various MPR levels (50%, 75%, 80%, 85%, 95%, and 99%). Consistent with our primary results, healthcare costs decrease monotonically as the MPR rises (Table 5). Second, we estimated regressions for the top 4 CHF drug subclasses (ranked by the proportion of patients with ≥1 fill) in the sample (ACE inhibitors, antianginals, β-blockers, and diuretics) using only the MPR calculated for that drug subclass. Results for this analysis were qualitatively similar to those of the main analysis.

A potential analytical limitation is that our measure of mean adherence depends on the number of CHF medica-

Table 4. Regression-Adjusted Healthcare Costs for Dual-Eligible and Non–Dual-Eligible Medicaid Beneficiaries by Medication Adherence[a]

	Dual-Eligible Beneficiaries, $			Non–Dual-Eligible Beneficiaries, $		
Variable	Adherent (n = 13,923)	Nonadherent (n = 10,690)	Difference	Adherent (n = 5989)	Nonadherent (n = 6806)	Difference
Total costs, including drug costs	24,506	32,419	–7913[b]	12,398	15,257	–2859[b]
Total costs, excluding drug costs	21,087	30,033	–8946[b]	9769	13,336	–3567[b]
Drug costs	3808	2491	1316[b]	3157	2124	1033[b]
Inpatient costs	9915	14,025	–4110[b]	4140	4826	–687[b]
Outpatient costs	8763	9867	–1104[b]	6334	8380	–2046[b]
Other costs[c]	2716	2750	–35	380	401	–21

[a]From the 1998 State Medicaid Research Files, the 1999 Medicaid Analytic eXtract, and the 1999 Medicare Standard Analytic File. Beneficiaries are classified as adherent if their medication possession ratio is 80% or higher.
[b]Significantly different from 0 at $P < .01$ (2-tailed t test).
[c]Include hospice, skilled nursing facility, home health, and emergency department

tions a patient fills. To test whether the association between healthcare costs and medication adherence varied among patients with differing numbers of unique drugs filled, we estimated regressions for the subgroups of patients with 1, 2, 3, and 4 or more unique CHF drugs filled. Across all 4 groups, results were qualitatively consistent with those of the main analysis (Table 5).

The final sensitivity analysis examined the decision to estimate the relationship between medication adherence and healthcare costs contemporaneously. Estimating models in this way cannot account for the potential of reverse causality that healthcare outcomes cause changes in medication adherence rather than vice versa. Although the results of this research do not suggest that better adherence results in fewer adverse health events and lower healthcare costs, the inclusion of healthy sample members who adhere regularly to medications and have few medical problems other than CHF might bias our results. To test this hypothesis, we examined 1998 healthcare use and estimated 4 separate models for patients with a (1) a Chronic Illness and Disability Payment System score of 1 or higher, (2) a diabetes diagnosis, (3) a diagnosis of coronary artery disease, and (4) hospitalization for any condition. For all 4 models, the association between the MPR and healthcare expenditures was qualitatively the same as that in the primary analysis.

DISCUSSION

In our study, higher medication adherence among Medicaid beneficiaries with CHF and those dually enrolled in Medicare was associated with a lower likelihood of hospitalization and ED use. This study's finding that adherent patients were slightly less likely to have a hospitalization is lower in magnitude than previous results among patients with CHF in which magnitudes were 8 to 10 percentage points[6] and 6.1% to 8.7%.[23] Findings on ED use were also lower in magnitude, although qualitatively similar.[8] Unlike other research on patients with CHF that did not find or did not examine other outcomes, this study also finds an association between CHF drug adherence and the number of hospitalizations, hospital days, and ED visits. That nonadherent beneficiaries are more likely than adherent beneficiaries to experience more of these adverse health events is likely important to state Medicaid agencies and to the federal government, as these events are expensive. Among patients in this research sample, the mean inpatient costs in 1999 among those with at least 1 visit were $19,432, or more than $6000 per visit. Given the persistent financial problems plaguing Medicare and the high mean cost of inpatient visits, improvement of CHF drug adherence among its beneficiaries (particularly dual eligibles) could result in considerable savings.

The relationship between CHF drug adherence and total costs was stark. When the MPR threshold of 80% was used, total costs for adherent patients were almost $6000 lower per year (Table 2). Although no other research has reported such a relationship for patients with CHF, one other study[6] found differences for commercially insured patients with hypertension and hypercholesterolemia.

This study also finds that the association between total healthcare expenditures and patient adherence is a graded one, challenging the 80% threshold used throughout the literature on medication adherence. Total healthcare costs of patients with adherence rates of 95% or higher were more than $3000 lower (almost 15%) than those of patients with adherence rates between 80% and less than 95% (Table 3). This result suggests that Medicaid agencies and the CMS could benefit substantially from interventions that improve beneficiaries' adherence to CHF drug therapy (as long as the

Table 5. Regression-Adjusted Sensitivity Analyses[a]

Healthcare Costs by Adherence to Specific Subclasses of CHF Drugs				
Drug Subclass	**Sample Size**	**Adherent, $**	**Nonadherent, $**	**Difference, $[b]**
Diuretics	23,925	21,247	23,763	–2516
ACE inhibitors	20,303	17,890	25,553	–7663
Antianginals	15,348	24,738	28,573	–3835
β-Blockers	12,013	17,978	25,695	–7717
Healthcare Costs by No. of CHF Drug Subclasses Patients Using				
No. of CHF Drug Subclasses Patients Using	**Sample Size**	**Adherent, $**	**Nonadherent, $**	**Difference, $[b]**
1	9419	13,638	19,783	–6145
2	9989	17,363	21,480	–4117
3	8552	18,761	27,774	–9013
≥4	9448	25,271	36,991	–11,720
Healthcare Costs by Medication Possession Ratio Level[c]				
Adherence Level, %	**Total Costs, Excluding Drugs, $**	**Total Costs, Including Drugs, $**	**Inpatient Costs, $**	**Outpatient Costs, $**
50	18,398	20,996	17,455	8196
75	15,866	18,761	14,800	7350
80	15,403	18,343	14,319	7192
85	14,953	17,934	13,854	7037
95	14,093	17,145	12,970	6737
99	13,763	16,838	12,632	6621

CHF indicates congestive heart failure.
[a]From the 1998 State Medicaid Research Files, the 1999 Medicaid Analytic eXtract, and the 1999 Medicare Standard Analytic File. Beneficiaries are classified as adherent if their medication possession ratio is 80% or higher.
[b]All significantly different from 0 at $P < .01$ (2-tailed t test).
[c]Estimated with the medication possession ratio specified as a continuous variable. Values represent cost estimates at these particular adherence levels.

cost of these interventions does not exceed their potential savings).

Total healthcare costs of patients with near-perfect medication adherence (≥99%) compared with patients whose medication adherence was slightly lower (95% to <99%) were about $1150 per year (6%) less than those of patients with slightly lower medication adherence (Table 3). Whether it would be cost-effective for Medicaid agencies or the CMS to encourage near-perfect adherence compared with adherence at least 95% of the time is dependent on how much more costly it is to these agencies to achieve near-perfect adherence rates among their beneficiaries. Future research should consider quantifying how much it might cost these agencies to improve medication adherence for patients with CHF who are already very adherent.

There are some limitations related to the use of administrative claims data and reverse causality. First, using pharmacy data to measure adherence can inform us that a prescription was filled but cannot confirm that patients take medications as directed. As in other medication adherence studies, we cannot account for this bias. Further research is needed on the association of patients' estimated medication adherence from claims with their reported adherence, possibly from surveys. Second, it was impossible to determine the severity of illness among patients with CHF by any means other than proxy measures. The association of medication adherence with healthcare utilization and costs might be different among patients having lower CHF severity compared with patients having higher severity. Future research should carefully address the association of CHF severity to inform policy makers of the risks of medication nonadherence among beneficiaries in the poorest of health. Third, our data did not allow us to account for important socioeconomic factors such as income or years of education. Because these factors are likely associated with drug adherence, their inclusion may have explained some of the variation in medication adherence across the sample. In particular, some research suggests that adherence to physician-recommended drug regimens (including adherence to a placebo) is associated with enhanced patient outcomes, indicating that researchers should

attempt (whenever feasible) to examine as many factors as possible when estimating the association between adherence and patient outcomes.[37-40]

An additional limitation to this study concerns our inability to determine whether it is truly medication adherence that is the only factor associated with lower healthcare utilization and costs. It is possible that patients who are adherent to medications are also adherent to other types of treatments (such as exercise and diet), but it is impossible with these data to assess adherence to these treatments. Further research should attempt to compare adherence to pharmaceutical and nonpharmaceutical therapies versus their joint association with healthcare utilization and costs.

Finally, because we measured medication adherence, healthcare use, and healthcare costs contemporaneously, our results might be biased by reverse causality that high healthcare costs could cause low medication adherence. However, the intent was not to suggest a direction of causality but merely an association. Moreover, if the primary results were biased in some way, we should expect to find no significant association between medication adherence and healthcare costs among patients in poor health at baseline. Yet, sensitivity analyses dispute this hypothesis.

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