

CHAPTER

7

**Measuring the effects of
medication adherence for the
Medicare population**

Measuring the effects of medication adherence for the Medicare population

Chapter summary

Medication adherence is viewed as an important component in the treatment of many medical conditions. Adherence to appropriate medication therapy can improve health outcomes and has the potential to reduce the use of other health care services. At the same time, improved adherence increases spending on medications. This issue has led to a proliferation of research on policies that encourage better adherence to medication therapy (e.g., reduced patient cost sharing) and the impact of improved medication adherence on health outcomes, typically measured by the use of other health care services.

Literature on medication adherence has found numerous policy interventions that can improve medication adherence. However, only a subset of these interventions relates better adherence to better health outcomes, patient satisfaction, and health care use and costs. Further, the long-term consequences are still uncertain (Goldman et al. 2007, Viswanathan et al. 2012).

This study builds on the analysis we conducted last year examining the relationship between adherence to medications and the use of medical services by Medicare beneficiaries with selected conditions. Our preliminary findings showed that the effects on Medicare spending of better adherence to medication therapies likely vary across medical conditions, medication regimens, and low-income subsidy (LIS) status. This variability suggests that

In this chapter

- Cohort selection
- Assignment of adherence levels
- Analytical approach
- Estimated effects of medication adherence
- Discussion

the results were not generalizable. Our findings also suggest that the reductions in spending we observed for the conditions we examined may not all have been attributable to improved adherence to medication therapies.

In this chapter, we examine how changes in cohort definitions and model specifications affect the estimated effects on medical spending from adhering to a medication therapy for Medicare beneficiaries with congestive heart failure (CHF).

The results of our analysis show the following:

- Better adherence to an evidence-based CHF medication regimen is associated with lower medical spending among Medicare beneficiaries with CHF, but the effects likely vary by beneficiary characteristics (e.g., age).
- Beneficiaries who follow the recommended CHF therapies tend to be healthier before being diagnosed with CHF than nonadherent beneficiaries, with fewer medical conditions and lower medical spending.
- The estimated effects of medication adherence on medical spending are highly sensitive to specifications in the estimation model. For example, including survivor status in the model reduced the effect on health care spending by half. The magnitude of the effect is also sensitive to how we define the adherent versus nonadherent population, and the criteria used to select the study cohort.
- The effects of medication adherence diminish over time.

Although our analysis examined only one condition (CHF) and is therefore not generalizable to other conditions or populations, the study findings highlight the difficulty in interpreting estimates of the effects of medication adherence as measured by spending differentials between adherent and nonadherent individuals. The difficulty may be exacerbated by the more-complex health profiles of the Medicare population compared with the general population often used in studies of medication adherence. ■

Background

Medication adherence is viewed as an important component of the treatment of many medical conditions. Adherence to appropriate medication therapy can improve health outcomes and has the potential to reduce the use of other health care services. At the same time, improved adherence increases spending on medications. This issue has led to a proliferation of research on policies that encourage better adherence to medication therapy (e.g., reduced patient cost sharing) and the impact of improved medication adherence on health outcomes, typically measured by the use of other health care services.

Literature on medication adherence finds numerous policy interventions that can improve medication adherence. However, only a subset of these policy interventions relates better adherence to better health outcomes, patient satisfaction, and health care use and costs. Further, the long-term consequences are still uncertain (Goldman et al. 2007, Viswanathan et al. 2012).

Studies that focus on individuals with certain chronic conditions have found that adhering to evidence-based medication therapy reduces the incidence of hospitalizations and emergency room visits (Goldman et al. 2007, Roebuck et al. 2011, Sokol et al. 2005). After reviewing recent research, the Congressional Budget Office (CBO) concluded that policies that change the cost-sharing structure of the Part D benefit probably affect federal spending on medical services. CBO plans to include medical spending offsets in future policy proposals that increase or decrease the use of prescription drugs covered under Part D (Congressional Budget Office 2012).

At the same time, there is a research gap in understanding the impact of improved medication adherence on health outcomes (Viswanathan et al. 2012). For example, there is lack of uniformity in how medication adherence is measured across studies. With adherence to most medication therapies decaying over time (typically within one year), the long-term effects of policies that encourage medication adherence are uncertain at best. Although experts generally agree that poor adherence to medications is a widespread phenomenon, the specific causes and solutions to the problem are less clear (Madden et al. 2008, Osterberg and Blaschke 2005, Schoenthaler et al. 2012, Viswanathan et al. 2012). CBO also points out that the effect of medication adherence on one of the key health outcomes—the mortality rate—has

not been well established, which could have important implications for estimating the budgetary effects of policy proposals that change the use of medications covered under the Part D benefit.

Preliminary findings from our own research show that the effects of better adherence to medication therapies on health outcomes as measured by Medicare spending vary across medical conditions, medication regimens, and low-income subsidy (LIS) status (Medicare Payment Advisory Commission 2013). For example, our estimates suggest that improved adherence among the least adherent beneficiaries with congestive heart failure (CHF) could result in lower medical spending, ranging from about \$860 to more than \$2,500 per beneficiary per year.¹ For other conditions, such as depression, we found almost no effects or an increase in Medicare spending from improved adherence. This variability in our findings across conditions, drug regimens, and populations suggests that the results are not generalizable and that the effects of improved adherence likely differ by medical condition, patient characteristics, and drug regimen.

Our findings also raise questions about whether the estimated effects could be confounded by factors unrelated to beneficiaries' medication-taking behavior that also affect their health. For example, we found that the effects on condition-specific costs (i.e., costs directly related to the condition being treated by study medications) accounted for relatively small portions of the overall effects for many of the study cohorts. In the case of beneficiaries with chronic obstructive pulmonary disease (COPD), medication costs for treating the condition exceeded the reductions in COPD-specific costs. We had anticipated that if medication adherence reduces expenditures on other health care services, it does so by affecting the condition targeted by the study drugs. We also found that a greater improvement in adherence did not necessarily result in a larger spending reduction compared with a more modest improvement in adherence.

Other findings raised questions about the validity of the methodology we used (and is often used by other studies) to define comparison groups based on observed level of adherence. A closer examination of individuals classified as adherent versus nonadherent revealed that some beneficiaries classified as having low adherence were often adherent to the study medications before experiencing medical events (typically inpatient admissions). We also found that some individuals were

switched to different study medication(s) during the observation period after some medical event, causing them to be classified as having low adherence even though they were adherent to the study medication(s) before the switch and may have continued to follow the new medication regimen after the switch.

As policymakers contemplate interventions to improve medication adherence, we need a better understanding of how medication adherence affects health outcomes and health care use for Medicare beneficiaries. Although not directly addressed in our study, this issue is important also because medication therapy could have negative effects on health outcomes if not used appropriately. For example, studies have shown that heavy use of medications, particularly in the elderly who are most likely to have multiple chronic conditions, increases the risk of having adverse drug reactions and drug–drug interactions (Lorgunpai et al. 2014, Routledge et al. 2004, Sarkar et al. 2011, Steinman et al. 2006). Thus, policymakers must use care in crafting policy interventions so that they do not inadvertently cause harm.

In this chapter, we explore the complexity involved in measuring the effects of medication adherence on medical spending, taking into account the heterogeneity we observed in our previous analysis, even among individuals who appeared to have a similar level of adherence. We examine how changes in cohort definitions and model specifications affect estimated effects of medication adherence on medical spending. We focus on Medicare beneficiaries with CHF primarily because the effectiveness of the evidenced-based treatment for CHF in improving health outcomes for patients with CHF has been well established in randomized clinical trials (Hunt et al. 2005).

Our study findings highlight the difficulty of interpreting the estimates of the effects of medication adherence as measured by spending differentials between adherent and nonadherent individuals. The difficulty may be exacerbated by the more complex health profiles of the Medicare population compared with the general population often used in the studies of medication adherence.

Cohort selection

For this study, we relied on diagnoses in medical claims to identify beneficiaries with CHF. Because of the

progressive nature of the disease, we applied an algorithm to limit the cohort to those in the early stage of the disease (i.e., those with a relatively new diagnosis of CHF).

We did not require possession of study medications to be included in the study cohort. However, we restricted the study cohort to those who were likely candidates for receiving at least one of the CHF medications.² For example, we excluded beneficiaries in hospice at any time before the initial diagnosis or those who entered hospice shortly after the diagnosis. Additional exclusions applied in selecting the study cohort included:

- beneficiaries residing in long-term care institutions in the three-month period before their qualifying event;
- beneficiaries for whom Medicare entitlement was based on disability; and
- beneficiaries who died at discharge or during an inpatient stay, if their qualifying event was in an inpatient setting.

Finally, beneficiaries were required to be continuously enrolled in fee-for-service Medicare (Part A and Part B) during the three-year period before the qualifying CHF event (or one-year period if they were 66 years or 67 years of age at the time of the qualifying event) and the three-year period after the qualifying event or until death. Beneficiaries also had to be continuously enrolled in Medicare Part D in the one-year period before the qualifying CHF event and the three-year period after the qualifying event or until death.

We used Medicare claims data from January 1, 2005, through December 31, 2010, for services covered under Part A and Part B and claims data from July 1, 2007, through December 31, 2012, for services covered under Part D. Medicare claims were linked with the Medicare Enrollment Database to create a longitudinal file that included demographic and Medicare enrollment characteristics, medical diagnosis, prescription drug use, and medical service use such as procedures, physician visits, home health and skilled nursing facility (SNF) care, and durable medical equipment (DME).

Identifying a CHF event using medical claims

A qualifying CHF event was identified using claims in the inpatient, outpatient (including emergency and nonemergency claims), and other settings, such as physician offices. To be included in the study, we required that a beneficiary have at least one inpatient claim with a

**TABLE
7-1**

Demographic and health characteristics by CHF medication use before and after qualifying CHF event

Demographic and health characteristics	CHF medication use pattern*			
	None before/ None after	None before/ Drugs after	Drugs before/ None after	Drugs before/ Drugs after
Number of beneficiaries	54,607	79,189	10,334	253,952
Percent of beneficiaries	14%	20%	3%	64%
Percent with qualifying CHF event in:				
Inpatient setting	56%	64%	56%	58%
Outpatient or other setting	44	36	44	42
Mean age at qualifying CHF event	82.3	80.8	82.1	80.8
Mean number of illness categories	2.1	1.7	3.4	2.3
Mortality rate				
60 days after qualifying CHF event	18.8%	2.3%	39.0%	5.3%
180 days after qualifying CHF event	24.0	3.9	47.8	7.5
3 years after qualifying CHF event	53.1	28.5	74.2	31.2

Note: CHF (congestive heart failure). Totals may not sum to 100 percent due to rounding.
*Medication use patterns based on the use of CHF medications during the six months preceding the qualifying CHF event ("before") and up to three years following the qualifying CHF event ("after").

Source: Acumen LLC analysis of Medicare data for MedPAC.

CHF diagnosis between January 1, 2008, and December 31, 2009, or at least two claims with a CHF diagnosis in outpatient or other settings, and no CHF claims in any setting in the three years before, so that only beneficiaries with a relatively new diagnosis were included in the cohort.³ For beneficiaries who were 66 years or 67 years old at the time of the qualifying CHF event, we required that there be no CHF claims in any setting for one year before the qualifying CHF event or since their enrollment in Medicare. About 60 percent of the qualifying CHF events were diagnoses recorded on an inpatient claim, while the remaining approximately 40 percent were based on diagnoses recorded on claims for outpatient or other settings (Table 7-1).

Patterns of CHF medication use

We considered CHF medications with strong evidence of clinical effectiveness (see online Appendix 7-A, available at <http://www.medpac.gov>). The medications fell into three major groups:

- angiotensin-converting enzyme (ACE) inhibitors;
- angiotensin receptor blockers (ARBs); and

- cardioselective beta-blockers and alpha- and beta-blockers.

We selected these medications because a number of randomized controlled trials have shown that ACE inhibitors, ARBs, and beta-blockers are effective in improving health outcomes for patients with CHF (Hunt et al. 2005). Some studies have suggested that appropriate use of these medications could reduce the use of other medical services (Goldman et al. 2007, Sokol et al. 2005).

A comparison of medication use before and after the qualifying CHF event suggested that identification of the study cohort based on medical claims diagnoses may not be reliable in identifying beneficiaries who were likely candidates for starting on CHF medications. For example, about two-thirds of beneficiaries were using CHF medications before their qualifying events, possibly for other cardiovascular conditions. Consequently, only a small proportion of beneficiaries who experienced a qualifying CHF event had newly started on CHF medications within six months after the event.⁴

Table 7-1 shows the distribution of beneficiaries across four different patterns of medication use before and after

the qualifying CHF event. The majority (64 percent) of the beneficiaries in the CHF cohort was already on CHF medications during the six-month period preceding the qualifying event (“drugs before”) and continued to take at least one CHF medication during the three-year period after the event (“drugs after”). Twenty percent started on a CHF medication regimen after the qualifying event, while 3 percent discontinued CHF medications after the qualifying event. The remaining 14 percent did not take any CHF medications either before or after the qualifying event (“none before/none after”).

Beneficiaries who were on CHF medications before the qualifying event (“drugs before” categories) had a greater number of illnesses, on average, compared with those who were not on CHF medications (“none before” categories). Most notably, we found higher incidences of hypertension among beneficiaries in “drugs before” categories (over 70 percent) compared with beneficiaries in “none before” categories (about 50 percent) (data not shown). We also observed much higher mortality rates among beneficiaries who did not start on CHF medications after the qualifying event. Beneficiaries who discontinued CHF medications after the qualifying event had the highest mortality, with nearly 40 percent dying within the first 60 days of the qualifying event. Nearly three-quarters died within three years of the qualifying event (Table 7-1, p. 129). Beneficiaries in the “none before/none after” category had the second highest mortality rate, with nearly 20 percent dying within the first 60 days and less than half surviving for more than three years after the qualifying event. Mortality rates were similar between beneficiaries who started on CHF medications after the event (“none before/drugs after”) and beneficiaries who continued on CHF medications after the event (“drugs before/drugs after”) by the end of the three-year period after the qualifying event.

The higher incidence of other medical conditions (mean number of illness categories), including hypertension in beneficiaries with prior CHF drug use (“drugs before”), compared with the rest of the cohort may complicate our measurements of the effects of CHF medication use on medical spending. Beneficiaries with more complex health profiles were likely to have higher medical spending that was unrelated to their CHF diagnosis. The higher mortality rates observed among the “none after” categories suggest that a larger share of beneficiaries in these categories were likely sicker than other beneficiaries in the CHF cohort, and many were already near the end of life at the time of the qualifying CHF event. Although it is possible that not adhering to the CHF medication regimen caused worse

health outcomes, the causality could also go the other way. That is, the poorer health status may account for the observed low adherence to CHF medications (“none after”) and higher medical spending before the CHF event (data not shown).

Because medications used to treat CHF are often used to treat other conditions—such as hypertension or other precursory risk factors—we began our analysis with a restricted cohort intended to limit the confounding effects of those preexisting health conditions. Thus, the first restriction we applied was to require that beneficiaries not be on CHF medications before the qualifying event (“none before”). We later examined the effects of excluding beneficiaries in the “none before/none after” category, the group with the second highest mortality rate, from the analysis.

Finally, it is possible that a CHF diagnosis on claims reflects screening and other diagnostic events rather than an actual diagnosis that warrants an initiation of a medication therapy, which may explain why some beneficiaries did not initiate medication therapy following a qualifying event. Such claims may be more likely in outpatient settings. In fact, we found that the proportion of beneficiaries newly starting on CHF medications after the qualifying event was somewhat higher among those beneficiaries whose identification was based on inpatient claims (21 percent) compared with those whose identification was based on claims from outpatient settings (about 18 percent). Thus, to be conservative, in our initial analysis, we further restricted the study cohort to beneficiaries who received their initial CHF diagnosis in an inpatient setting (second restriction).

Our initial study cohort consisted of 80,719 beneficiaries. These beneficiaries were in one of the two “none before” categories and received their initial CHF diagnosis in an inpatient setting (56 percent of the “none before/none after” category and 64 percent of the “none before/drugs after” category). Later, we relaxed these restrictions and reported the results of the analyses based on three variations of the study cohort.

Assignment of adherence levels

We examined the medication use patterns in the initial (restricted) study cohort (80,719 beneficiaries)—i.e., beneficiaries with qualifying CHF events in the inpatient

setting with no CHF drug use in the six months before the qualifying event. We defined *adherence* as possessing any of the study medications based on Part D prescription drug event data and determined whether a beneficiary was classified as adherent or not adherent on a monthly basis.⁵ This definition allowed beneficiaries to be treated as adherent when their medication(s) were changed to another CHF medication (or medications) for clinical reasons.

We assigned the study cohort to one of three groups based on the level of adherence. Beneficiaries starting on any of the CHF medications within three months of the qualifying event and continuing on any of the CHF medications for at least six months were assigned to the high-adherence group. Those who started on CHF medications within three months of the qualifying event but discontinued using CHF medications within six months of the initiation of the therapy were assigned to the low-adherence group. Finally, those who either did not start on CHF medications after a qualifying event or started on CHF medication(s) more than three months after the qualifying event were classified in the nonadherent group.

Less than half (45 percent) of the beneficiaries (high- and low-adherence groups combined) in this restricted cohort started on at least one of the CHF study medications within three months of the qualifying event (Table 7-2, p. 132). About 70 percent of those (32 percent of the study cohort) continued to take the CHF medications for at least six months (high-adherence group). The other 30 percent (13 percent of the study cohort) discontinued within six months of the initiation of the medication therapy (low-adherence group). The remaining 55 percent did not start on CHF medications after a qualifying event, or they started on CHF medication(s) more than three months after the qualifying event (nonadherent group).

Most studies of medication adherence use the proportion of days covered (PDC) metric as a proxy for medication adherence. We measured the PDC in our study cohort during the six months after the qualifying CHF event. The PDC averaged about 83 percent among beneficiaries in the high-adherence group, about 38 percent among beneficiaries in the low-adherence group, and about 4 percent among beneficiaries in the nonadherent group. The majority (89 percent) of beneficiaries in the nonadherent group did not start on CHF medications within six months of the qualifying event. Among the 11 percent who did start on CHF medications, the PDC averaged about 30 percent. A PDC at or above 80 percent is typically considered adherent to a given drug therapy.⁶

Characteristics of beneficiaries by adherence levels

We found that beneficiaries with different adherence levels also differed in ways that may have affected their ability to adhere to a medication therapy. Table 7-2 (p. 132) presents demographic and health characteristics of the CHF study cohort at baseline (i.e., during the six-month period before the qualifying CHF event) by the level of adherence to study medications. Beneficiaries in the nonadherent group tended to be older and have higher incidence of illnesses, such as chronic obstructive pulmonary disease, specified heart arrhythmias, cancer, and renal failure, compared with beneficiaries in the other two groups (high- and low-adherence groups).

Average monthly medical spending and use per person during the six-month period before the qualifying event also suggests beneficiaries in the nonadherent group had poorer health status, on average, compared with those in the high- and low-adherence groups before the qualifying event. Medicare spending per month averaged over \$1,500 among beneficiaries in the nonadherent group, compared with \$1,144 among those in the low-adherence group and less than \$1,000 among those in the high-adherence group. The difference in average Medicare costs was driven primarily by the higher rates of inpatient admissions among beneficiaries in the nonadherent group compared with the other two groups. Beneficiaries in the nonadherent group also had more physician office visits compared with the other groups (4.7 visits per beneficiary compared with 3.9 and 4.4 visits per beneficiaries for high- and low-adherence groups, respectively).

Finally, the higher short-term (180 days after the qualifying CHF event) and long-term (1 year and 3 years after the qualifying CHF event) mortality rates among beneficiaries in the nonadherent group compared with those in high- and low-adherence groups also suggests poorer health status among beneficiaries in the nonadherent group compared with beneficiaries in the other groups. Notably, the short-term mortality rate among beneficiaries in the low-adherence group (3.2 percent) was lower compared with that observed among beneficiaries in the high-adherence group (7.2 percent). However, that relationship was reversed at the one-year mark after the qualifying event. It is not clear whether this change reflects effects of better adherence to medication therapy or differences in prior health status (Table 7-2, p. 132).

**TABLE
7-2**

Demographic and health characteristics of beneficiaries in the CHF study cohort by adherence group

Beneficiaries in CHF study cohort by level of adherence

Demographic and health characteristics	Adherent		
	High adherence	Low adherence	Nonadherent
Number of beneficiaries	25,921	10,212	44,586
Percent of beneficiaries	32%	13%	55%
Proportion of days covered	83%	38%	4%
Age at qualifying CHF event date			
Mean	81	81	82
By age category (in percent)			
70 or younger	11%	10%	8%
71–80	34	33	30
81–85	22	23	22
86 or older	33	34	40
Percent:			
Female	64%	61%	65%
White	88	83	87
Receiving the low-income subsidy	65	61	62
Residing in urban areas	33	31	33
Mean number of illness categories	1.5	1.7	2.0
Percent with selected illnesses			
Diabetes	19%	21%	21%
Chronic obstructive pulmonary disease	16	19	25
Specified heart arrhythmias	15	16	19
Cancer	11	12	14
Renal failure	8	11	12
Stroke	4	4	6
Baseline average health care use			
Medicare costs per month	\$978	\$1,144	\$1,528
Number of inpatient admissions per 1,000	213	261	366
Inpatient days per admission	5.2	5.3	5.7
Number of physician office visits per beneficiary	3.9	4.4	4.7
Mortality rate			
180 days after qualifying CHF event	7.2%	3.2%	17.8%
1 year after qualifying CHF event	19.3	23.7	34.0
3 years after qualifying CHF event	40.7	48.2	56.1

Note: CHF (congestive heart failure). Totals may not sum to 100 percent due to rounding.

Source: Acumen LLC analysis of Medicare data for MedPAC.

Analytical approach

We began our analysis using the restricted cohort of beneficiaries identified as having had a CHF event in

the inpatient setting, with no prior CHF medication use (the initial cohort of 80,719 beneficiaries). Even within this restricted cohort, the demographic and health characteristics of beneficiaries differed across the beneficiaries with different levels of adherence to

medication use. Our analyses explored how different model specifications, selected beneficiary characteristics such as age and low-income subsidy (LIS) status, and criteria used to select the study cohort affected the estimated effects of better adherence.

We used a multivariate regression model to estimate medical spending over two outcome periods, the first six months (months 1 through 6) and the following six months (months 7 through 12) after the qualifying CHF event. We fitted the following ordinary least squares regression model to compare medical spending across the three adherence groups:

$$Y_i = \alpha + Y_1 \text{High Adherence}_i + Y_2 \text{Low Adherence}_i + \beta_1 X_i + \varepsilon_i$$

where Y_i is the average medical spending per month for beneficiary i , adjusted for the number of days alive. “High Adherence” and “Low Adherence” are dummy variables corresponding to our high- and low-adherence groups, respectively. The nonadherent group serves as the reference group. Estimates Y_1 and Y_2 indicate spending differentials for the two adherence groups relative to the nonadherent group. Depending on the model, X includes sociodemographic characteristics, comorbid conditions, medical spending, and drug use patterns before the qualifying event, and indicators for survival status at 6 months and 12 months after the CHF event. A complete list of covariates is provided in the appendix (see online Appendix 7-B, available at <http://www.medpac.gov>).

Estimated effects of medication adherence

The effects of medication adherence are typically measured by comparing the medical spending of the adherent population to the nonadherent population and attributing the difference in the spending levels to health outcomes resulting from adhering to medication therapies (Cole et al. 2006, Lynch et al. 2009, Roebuck et al. 2011, Sokol et al. 2005). The results reported are effects on Medicare Part A and Part B spending and do not net out the costs of medications to Part D. Because CHF medications included in this study are in classes with many generic substitutes, the cost of adhering to medications was relatively low, ranging from a few dollars to slightly over \$20 per month, on average, depending on

the level of adherence. Netting out the Part D costs does not materially change our findings.

Comparison across different model specifications

We estimated the effects of better medication adherence on medical spending for the initial study cohort using the following six model specifications:

1. adherence-group indicators;
2. adherence-group indicators and sociodemographic characteristics (excluding race);
3. adherence-group indicators and sociodemographic characteristics (including race);
4. adherence-group indicators, sociodemographic characteristics (excluding race), comorbidities, and drug use patterns at baseline;
5. adherence-group indicators, sociodemographic characteristics (excluding race), comorbidities, drug use patterns at baseline, and medical spending at baseline; and
6. adherence-group indicators, sociodemographic characteristics (excluding race), comorbidities, drug use patterns at baseline, medical spending at baseline, and survival status indicators.

Table 7-3 (p. 134) shows the difference in average monthly medical spending between the adherent groups (high- and low-adherence groups) and the nonadherent group for the six model specifications described above. The estimated medical spending effects during the first six months after the qualifying CHF event (outcome period 1) were lower among the adherent beneficiaries compared with those of nonadherent beneficiaries for all six model specifications. The estimated effects generally declined as more variables were added to control for differences in beneficiary characteristics and health status, as measured by baseline health care use, across the three groups. For example, among beneficiaries with high adherence, the estimated effects went down from \$5,142 for the specification with no adjustment for beneficiary characteristics or health status (specification 1) to \$4,869 when the model controlled for sociodemographic characteristics, comorbidities, and patterns of medication use (specification 4). However, we found that adding sociodemographic characteristics (with or without race) had very little effect on the estimated spending differentials (specification 2 and specification 3).

**TABLE
7-3**

Estimated average monthly medical spending differentials between beneficiaries in adherent groups and nonadherent group, by outcome period

Model specification	Difference between nonadherent group and:			
	High-adherence group		Low-adherence group	
	Months 1-6	Months 7-12	Months 1-6	Months 7-12
1: Adherence indicator	-\$5,142*	-\$839*	-\$4,178*	\$326*
2: Model 1 + sociodemographic characteristics (excluding race)	-5,058*	-804*	-4,313*	244
3: Model 1 + sociodemographic characteristics (including race)	-5,062*	-803*	-4,337*	219
4: Model 2 + comorbidities + drug use pattern at baseline	-4,869*	-485*	-4,185*	459*
5: Model 4 + medical spending at baseline	-4,783*	-387*	-4,128*	500*
6: Model 5 + survival status indicators	-2,620*	-124	-2,270*	391*

Note: "Months 1-6" refers to the first six months after the qualifying congestive heart failure (CHF) event (outcome period 1), and "months 7-12" refers to the second six months after the qualifying CHF event (outcome period 2).
*Denotes statistical significance at the 5 percent level.

Source: Acumen LLC analysis of Medicare data for MedPAC.

We found that adding survival status indicators had the largest effect, reducing the estimated effects by nearly half (to \$2,620) (specification 6). Similar patterns were observed for beneficiaries with low adherence, though the estimated effects were somewhat smaller for all model specifications compared with those observed for the high-adherence group.

For the second six months after the qualifying event (outcome period 2), the estimated spending differentials were much smaller for the high-adherence group compared with those observed during outcome period 1. The spending effect was no longer statistically significant once the survival status indicator was added (specification 6). For beneficiaries in the low-adherence group, we found that estimated spending was consistently higher (though not always statistically significant) compared with the spending levels observed among beneficiaries in the nonadherent group.

Comparison between subgroups

We conducted two subgroup analyses using specification 6 that included the full set of covariates. In the first subgroup analysis, we stratified the beneficiaries into those who were 80 years of age or younger and those who were over 80 years of age to assess the estimated effects of medication use by age. In the second subgroup analysis, we stratified the beneficiaries by their LIS status to assess

whether the estimated effects of medication use differed between LIS and non-LIS beneficiaries.

The magnitude of the spending differentials between adherent (high- and low-adherence groups) and nonadherent beneficiaries during outcome period 1 was larger for individuals over 80 years of age compared with those who were 80 years of age or younger (Table 7-4). The spending differentials were not statistically significant for outcome period 2, with the exception of older beneficiaries (over 80 years of age) with low adherence, where medical spending, on average, exceeded that of the nonadherent beneficiaries by \$644 per month.

The spending differentials between adherent and nonadherent beneficiaries were larger among individuals receiving the LIS compared with those who did not receive the LIS during outcome period 1 (Table 7-4). But those spending differentials did not persist beyond the first six months, with the exception of LIS beneficiaries with relatively low adherence. Their medical spending exceeded that of the nonadherent beneficiaries receiving the LIS by \$710 per month, on average.

Comparison across different cohort selection criteria

We examined whether the definitions used to identify the study cohort affected the estimated spending effects of medication adherence. For this analysis, we used three variations on the definition of the study cohort and

**TABLE
7-4**

Estimated average medical spending differentials among subgroups of beneficiaries in adherent groups and nonadherent group, by outcome period

Subgroups	Difference between nonadherent group and:			
	High-adherence group		Low-adherence group	
	Months 1-6	Months 7-12	Months 1-6	Months 7-12
All beneficiaries	-\$2,620*	-\$124	-\$2,270*	\$391*
By age				
≤ 80 years of age	-2,108*	-283	-1,992*	62
> 80 years of age	-2,927*	43	-2,444*	644*
By LIS status				
LIS	-3,060*	-163	-2,648*	710*
Non-LIS	-2,366*	-116	-2,061*	198

Note: LIS (low-income subsidy). "Months 1-6" refers to the first six months after the qualifying congestive heart failure (CHF) event (outcome period 1), and "months 7-12" refers to the second six months after the qualifying CHF event (outcome period 2).

*Denotes statistical significance at the 5 percent level.

Source: Acumen LLC analysis of Medicare data for MedPAC.

compared the results for model specification 6 (see online Appendix 7-C, available at <http://www.medpac.gov>).

The first variation excluded from the nonadherent group those individuals who did not start on CHF medications within six months of the qualifying CHF event. This variation was equivalent to defining the study cohort based on possession of study medication(s) during a specified time period. We found spending differentials were larger for both the high- and low-adherence groups when we excluded individuals with no CHF medication use (see online Appendix 7-C, available at <http://www.medpac.gov>). This finding is somewhat puzzling and may require further investigation. If the measured effects truly reflect the effects of taking CHF medications, this finding would imply that—at least for those in the nonadherent group—health outcomes were worse for those who started on CHF medications compared with those who did not. One possible explanation is that many individuals who started on CHF medication(s) experienced adverse drug reactions from one or more medications, which would explain the greater use of health care services as well as low adherence. The second variation expanded the study cohort to include beneficiaries who were on CHF medications before the qualifying event ("drugs before/ drugs after" and "drugs before/none after" categories),

and the third variation included individuals for whom the qualifying CHF events were in a noninpatient setting (such as a hospital outpatient department or a physician's office). The results show that estimated effects are sensitive to the criteria used to select the study population (see online Appendix 7-C).

Discussion

In this study, we examined whether and how the relationship between medication adherence and medical spending varied by the model specification we chose, how we defined the adherent population versus nonadherent population, and the criteria we used to select the study cohort. One goal was to understand the complexity involved in defining the study cohort. Our other goal was to measure how sensitive the estimated effects of medication adherence on medical spending were to the definition used to select the study cohort and the model specification used for the analysis. We chose CHF because the effectiveness of the evidence-based CHF treatment in improving health outcomes has been well established in randomized clinical trials, and thus, Medicare beneficiaries with CHF would be expected to benefit the

most from improved medication adherence by preventing complications that result in inpatient admissions, thereby reducing overall medical costs (Goldman et al. 2007, Hunt et al. 2005, Roebuck et al. 2011, Sokol et al. 2005).

Our primary finding is that better adherence to an evidence-based CHF medication regimen is associated with lower medical spending among Medicare beneficiaries with CHF. A comparison of unadjusted Medicare spending across the adherence groups suggests that the spending effects are driven primarily by fewer inpatient admissions and skilled nursing facility days among the beneficiaries in the adherent groups compared with the nonadherent group during the first six months after the CHF event. A closer examination of the medical service use during the outcome period may provide insight into the relationship between the baseline health status, medication-taking behavior, and the medical service use after the CHF event.

Although we find an association between medication adherence and lower medical spending, the estimated effects on medical spending were sensitive to the methodology used to measure the effects, and those effects diminish over time. For example, including an indicator for survival status reduced the estimated effects by nearly half. We also find that using different criteria to select the study cohort results in different estimates of the spending effects. Further, our subgroup analyses suggest that estimated spending effects vary by age and LIS status, and likely by other individual characteristics, such as institutionalized status.

The likely existence of selection bias among adherent and nonadherent beneficiaries not observable in administrative data makes it difficult to interpret the results. A comparison across beneficiaries with different levels of adherence suggests that beneficiaries who were following the guideline CHF medication regimen tended to be healthier than nonadherent beneficiaries, with fewer medical conditions and lower medical spending in the period preceding a CHF event and lower mortality rates after the CHF event. Thus, our estimated effects could reflect the benefit of adhering to the recommended medication therapy, or it may reflect, for example, physicians' decisions about the appropriate treatment given the health status of their patients. Patients themselves could also differentially self-select whether to follow the recommended medication regimen, which may be correlated with behaviors or attitudes that affect their

health and influence medical spending independent of their medication-taking behavior.

Despite an attempt to adjust our estimates for the possibility of this selection bias, our findings suggest that controlling for observed differences in beneficiary characteristics may not be sufficient to fully account for the effects of selection bias. For instance, we initially applied restrictive criteria—intended to select only individuals who were candidates for starting on a guideline CHF medication treatment—for inclusion in the study cohort. However, even with this restricted cohort, we find that our estimate of the effects of medication adherence on medical spending is sensitive to model specifications, particularly when we add variables that measure differences in health status, such as comorbidities, prior medical spending, and drug use patterns. Sociodemographic characteristics, on the other hand, had very little influence on estimated spending effects.

Adding information on mortality to our fully specified model—which already included sociodemographic factors, comorbidities, and prior medical spending and patterns of drug use—had the greatest effect. Estimates based on model specifications that did not include short-term mortality (survival status within six months of the CHF event) suggested that medical spending for adherent beneficiaries was lower than that of nonadherent beneficiaries by \$4,000 to \$5,000 per month, on average. Including the survival indicator reduced that estimated “saving” by nearly half.

This finding highlights the difficulty involved in adjusting for health and other differences between adherent and nonadherent individuals using factors that can be observed (i.e., in administrative data). While the average medical spending per month is adjusted for the number of days alive, high spending near the end of life likely contributed to the larger spending effects in models that do not include survival status indicators. It is possible that the higher mortality rate observed among individuals in the nonadherent group is the result of not taking CHF medications. That is, the inclusion of the survival status is causing an endogeneity problem that may require the use of other econometric techniques such as instrumental variables. It is also possible that mortality, particularly in the short term, is capturing some of the differences in health status that were not captured by other health status variables in the model. Although determining the extent to which health status variables, such as survival status, are correlated with medication adherence is beyond the scope

of this study, we note that this issue may be exacerbated by the more complex health profiles of the Medicare population compared with the general population often used in the studies of medication adherence.

Finally, the results consistently show that effects of medication adherence diminish over time. We found striking differences in the estimated spending effects during the first six months after the qualifying CHF event (outcome period 1) compared with the second six months after the event (outcome period 2). For example, the estimated spending differential for beneficiaries with a relatively high adherence suggests that adhering to the CHF medication regimen lowers medical spending by nearly \$5,000 per month on average during outcome period 1, compared with about \$400 to \$800 during outcome period 2. Accounting for the difference in the mortality rates reduced the outcome period 1 estimate to about \$2,600, which is still much larger than the corresponding estimate for outcome period 2 (\$124). In the case of beneficiaries with relatively low adherence, the estimated spending effects were positive, indicating higher medical spending relative to those who were nonadherent. This pattern was consistent across all model specifications and cohort definitions.

These findings further complicate the interpretation of spending differentials between adherent and nonadherent individuals. Does lower spending during outcome period 1 represent lower medical spending resulting from better

adherence to CHF medication regimen? If so, why does most of that effect disappear in outcome period 2? Alternatively, does it reflect differences in health status that existed before the CHF event? If so, what explains the reversal in the effects for some cohorts in outcome period 2?

Although our analysis examined only one condition (CHF) and is therefore not generalizable to other conditions or populations, this study underscores the complexity involved in estimating the effects of medication adherence. Our findings suggest that one must use caution when using administrative data to estimate the effects of medication adherence. This study also highlights many gaps in our understanding of how medication adherence affects health care spending and use. For example, we need a better understanding of why adherence decays within a relatively short period of time and how that may affect the short-term and long-term effects of adhering to medication therapies.

As policymakers consider interventions to increase adherence to medication therapies, we need a better understanding of how the effects of medication adherence vary by condition and by population subset, particularly if the population includes vulnerable individuals with multiple chronic conditions. More research is needed to determine clinical conditions for which medication adherence improves health outcomes so that efforts to improve adherence can be focused on those conditions. ■

Endnotes

- 1 These findings are for beneficiaries with a diagnosis of CHF based on CMS's prescription drug hierarchical condition category, used to assign risk scores to each Part D enrollee. To avoid including beneficiaries at a very advanced stage of CHF, we limited the study cohort to those with no claims for implantable cardioverter-defibrillators or biventricular pacemakers.
- 2 The new cohort selection criteria differed from the one used for our previous analysis. First, we no longer required that a beneficiary fill the study medication(s) during the observation period. Instead, the new criteria were designed to select those who were likely to have been prescribed one of the CHF medications. Second, instead of relying on claims for implantable cardioverter-defibrillators or biventricular pacemakers to determine the severity of the disease (because CHF is a progressive disease), we selected only those who were newly diagnosed with CHF so that individuals included in the study cohort were likely to be at an early stage of CHF.
- 3 The International Classification of Diseases, Ninth Revision, Clinical Modification codes used to identify CHF diagnosis were 428, 4280–4282, 42820–42823, 4283, 42830–42833, 4284, 42840–42843, 4289, 40211, 40291, 40411, and 40491.
- 4 We considered beneficiaries to have newly started on CHF medications if they did not have any CHF medication use during the six-month period preceding the qualifying CHF event and started on at least one CHF medication within six months after the qualifying event.
- 5 Because we are using administrative data to measure medication adherence, we relied on a possession of study medication(s) to measure adherence, which is an imperfect measure since people may not take all the medications they obtain.
- 6 A PDC threshold of 0.8 (80 percent) is endorsed by the Pharmacy Quality Alliance and is commonly used by health services researchers.

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