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Medication Adherence Leads To Lower Health Care Use And Costs Despite Increased Drug Spending

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ABSTRACT **Researchers have routinely found that improved medication adherence—getting people to take medicine prescribed for them—is associated with greatly reduced total health care use and costs. But previous studies do not provide strong evidence of a causal link. This article employs a more robust methodology to examine the relationship. Our results indicate that although improved medication adherence by people with four chronic vascular diseases increased pharmacy costs, it also produced substantial medical savings as a result of reductions in hospitalization and emergency department use. Our findings indicate that programs to improve medication adherence are worth consideration by insurers, government payers, and patients, as long as intervention costs do not exceed the estimated health care cost savings.**

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Almost half of all Americans, approximately 133 million people, live with at least one chronic disease.[1] Because ongoing use of prescription medication is a key component of treatment for chronic conditions, medication adherence—or making sure that patients take the drugs prescribed for them—is a matter of great importance to policy makers, insurance plan sponsors, physicians, and patients.

Patients who adhere to their medication regimens enjoy better health outcomes[2,3] and make less use of urgent care and inpatient hospital services, compared to patients with similar medical conditions who are not adherent.[4,5] Yet despite the evidence of improved outcomes from adherence, the World Health Organization reports average medication compliance rates in developed countries of just 50 percent.[6]

By definition, improvements in medication adherence increase pharmacy spending. Health care reformers and payers are therefore interested in knowing whether or not the higher pharmacy costs are more than offset by reductions in the use of medical services. If so, the financial benefit may justify adopting programs that promote compliance or that remove barriers to adherence.

Given the widespread policy debate over how best to bend the health care cost curve downward, it is surprising that medication adherence by patients with chronic diseases does not feature more prominently in the conversation. However, as we discuss in this article, research into medication compliance suffers from methodological challenges that may call the validity of the results into question.[5,7,8] This could explain the lack of discussion in the health policy arena about the value of medication adherence.

Research in this area focuses on chronic conditions that are highly prevalent, costly, or both. These include asthma, congestive heart failure, depression, diabetes, epilepsy, gastrointestinal disorders, hypertension, osteoporosis, schizophrenia, and dyslipidemia (high levels of "bad" cholesterol).

To date, investigators have routinely found improved adherence to be associated with lower total health care costs.[9–12] Notable exceptions include depression, osteoporosis, and asthma—conditions in which adherence has sometimes

been associated with increases in overall costs, perhaps because of the dominance of brand-name, and thus more expensive, medications in the treatment of these conditions.[13–15] Reductions in hospitalizations and emergency department visits are overwhelmingly reported to be the key drivers of declining health care costs associated with improved medication adherence.

However, these prior studies have a common limitation: the inability to establish a causal link between the key explanatory variable—medication adherence—and the outcomes of interest, such as hospitalizations and total health care costs. This limitation springs from the use of an observational research design, as opposed to a randomized controlled trial.

Observational research can never reveal if individuals in the groups being compared differ in ways that are not observed. If an unobserved and unmeasured trait is related to both the characteristic that differentiates the groups—the explanatory variable—and the outcome being examined, then the trait may bias the results. This problem, known as endogeneity, plagues the published literature on the relationship between medication adherence and health services use and cost. One example of this sort of bias is known as the "healthy user effect": the tendency of people who more closely follow their medication regimens to also engage in such health-enhancing behavior as exercising regularly and eating a healthy diet.[16]

This article examines the relationship between medication adherence and the use and cost of health services in patients who had one or more of the following four chronic vascular conditions: congestive heart failure, hypertension, diabetes, and dyslipidemia. We analyzed a large panel data set and used an advanced econometric technique that addresses the endogeneity problem by mathematically eliminating unmeasured confounding variables if they did not change over time. Our combination of data and methods allowed us to move from possibly uncovering statistical associations to more confidently inferring causal links between medication adherence and the use and cost of health care.

We also investigated whether or not medication adherence had a differential impact on health outcomes depending on patients' sex or age. Specifically, we compared people under age sixty-five with older patients, given that people age sixty-five and older make up a particularly important cohort in light of their eligibility for Medicare. Our findings revealed robust reductions in emergency department visits and inpatient hospital days as a result of medication adherence. Consequently, adherence leads to total health care cost savings. We conclude by commenting on the implications of these findings in the context of health care reform.

Study Data And Methods

STUDY SAMPLE As one of the largest pharmacy benefit managers in the United States, CVS Caremark adjudicates prescription drug claims for its clients: sponsors of health insurance plans. For this study we extracted integrated pharmacy and medical administrative claims data from the CVS Caremark data on people who had continuous health insurance coverage sponsored by one of nine US employers from January 1, 2005, through June 30, 2008.

We used primary, secondary, and tertiary *International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM), codes to construct cohorts of patients with the four targeted conditions. We selected patients who had at least two outpatient visits on different dates, or one hospitalization or emergency department visit, with a specified ICD-9-CM code (see Appendix Table A1).[17] We included subjects in more than one disease cohort if they met our inclusion criteria (see Appendix Table A2 for the extent of the overlap).[17]

After we used the first six months of data to properly calculate the adherence measures, as described below, our analytical data set consisted of a panel of 135,008 individuals, each with three consecutive yearly observations (July 1, 2005–June 30, 2006; July 1, 2006–June 30, 2007; and July 1, 2007–June 30, 2008). The final sample included 16,353 patients with congestive heart failure, 112,757 with hypertension, 42,080 with diabetes, and 53,041 with dyslipidemia.

STUDY VARIABLES The empirical analysis included three measures of health services use: annual numbers of inpatient hospital days, emergency department visits, and outpatient physician visits. It also included three measures of health services cost: annual pharmacy, medical, and total health care costs. All six of these dependent variables applied to all medical causes, not just the specific diseases we studied.

We used data on coordination of benefits so that the cost measures would comprise contributions from all payers, including plan sponsors, members, and other insurers such as Medicare. The inclusion of nine different payers decreased the study's sensitivity to potential differences in the employers' pharmacy and medical benefits.

Pharmacy costs consisted of ambulatory prescriptions dispensed by outpatient, community-based, or mail-service pharmacies. We derived

medical costs from medical claims. Total health care costs represented the sum of pharmacy and medical costs.

We measured adherence using the medication possession ratio (MPR). A common metric in pharmacoeconomics and outcomes research, this ratio uses pharmacy claims data to derive the proportion of time that a patient has medication on hand to treat a specific condition.

In our study, for every therapeutic class of drug used to treat each chronic condition (see Appendix Table A1),[17] we calculated a patient's medication possession ratio for each of the three yearly observations as the number of days during the year when the patient had medication, divided by the number of days in the year. For example, a patient who had a supply of medication for a total of 255 days in a given year would have had a medication possession ratio of 0.70 (255 days of possession divided by 365 days).

We consulted pharmacy claims during the first six months of our study (January 1 through June 30, 2005) to "credit" the patient's first medication possession ratio with medication on hand as of the beginning of the first observation year. Subsequent calculations carried leftover medication from year to year. Therefore, MPR values ranged from 0 to 1.

Next, we derived condition-level adherence for each patient-year observation. We calculated this as the average of the medication possession ratios for all therapeutic classes for each chronic disease, weighted by the days' supply in each therapeutic class (see Appendix Table A1).[17] For patients who had been diagnosed with a chronic condition but had not yet received any medication for it, we used a condition-level medication possession ratio of 0.

Finally, we constructed a dichotomous variable for adherence for each of the four vascular conditions. We considered a condition-level medication possession ratio below 0.80—a threshold commonly used by researchers—to be nonadherent, and a ratio of 0.80 or greater to be adherent. Again, we created this variable for each patient-year observation. For a more detailed discussion of the derivation of our adherence measure, see Appendix Section 1.[17]

In addition to the indicators of adherence, we used dichotomous variables for age, depending on whether or not the patient was sixty-five or older (as of the first day of each year), and sex, using pharmacy benefit eligibility records. To control for the presence of other diseases, we derived the Charlson Comorbidity Index for each year.[18–20] We also included time dummy variables to control for concurrent trends in health services use and cost, such as drug price inflation, expansions in the availability of generic drugs, and advances in health care technology.

STATISTICAL ANALYSIS We estimated condition-specific models for each of the six dependent variables, for a total of twenty-four models. The endogeneity of adherence in these models was a key methodological concern in our analysis. Consequently, as previously described, we used linear fixed-effects modeling to handle this potential problem. To examine differential effects of adherence, we also added interactions between adherence and sex and age group to the models.[21] We used the statistical software Stata, version 11.1.

LIMITATIONS Our study had various limitations. First, we did not analyze the timing of adherence effects on health services use and cost. Because many patients in our analytical data set may have been long-term users of their vascular medications, the estimated impacts of adherence could represent cumulative rather than instantaneous effects. In other words, one should not necessarily expect to see immediate reductions in medical costs from improved medication adherence. This is a particularly salient point for insurers with short time horizons.

Second, we advise against adding together estimates of condition-specific effects for patients with more than one vascular disease. Such addition could double-count reductions in health services use and cost resulting from adherence.

Third, the study sample was a relatively large and demographically diverse set of patients insured by their employers, and the group age sixty-five and older included both active employees and retirees. Moreover, we analyzed both existing and new cases of vascular disease. Despite these broad inclusion criteria, our results might not be generalizable to all populations.

Finally, although our econometric method addressed the potential endogeneity of adherence largely ignored in prior studies,[22] fixed-effects modeling is still not as good as a randomized controlled trial in establishing causality.[23]

Results

With regard to sample characteristics, we found that males constituted a somewhat higher proportion of the congestive heart failure (55 percent) and diabetes (53 percent) cohorts than did females, whereas the dyslipidemia (50 percent) and hypertension (51 percent) groups were more evenly balanced by sex. Congestive heart failure patients tended to be older (average: 77 years) than patients with the other three conditions (averages: 65–68 years).

Average medication possession ratios varied across the four conditions: Congestive heart failure patients had the lowest (0.40), and patients

with hypertension had the highest (0.59). Adherence rates ranged from 34 percent to 51 percent.

Congestive heart failure patients spent an average of 11.90 days in the hospital per year, compared to 3.29 days for patients with hypertension, 4.26 days for those with diabetes, and 2.24 days for those with dyslipidemia. Total health care costs per patient per year averaged $39,076 for congestive heart failure, $14,813 for hypertension, $17,955 for diabetes, and $12,688 for dyslipidemia. Pharmacy costs (for all prescriptions filled, not just those for the four chronic vascular conditions) ranged from $2,867 to $3,780 per patient per year (see Appendix Table A3).[17]

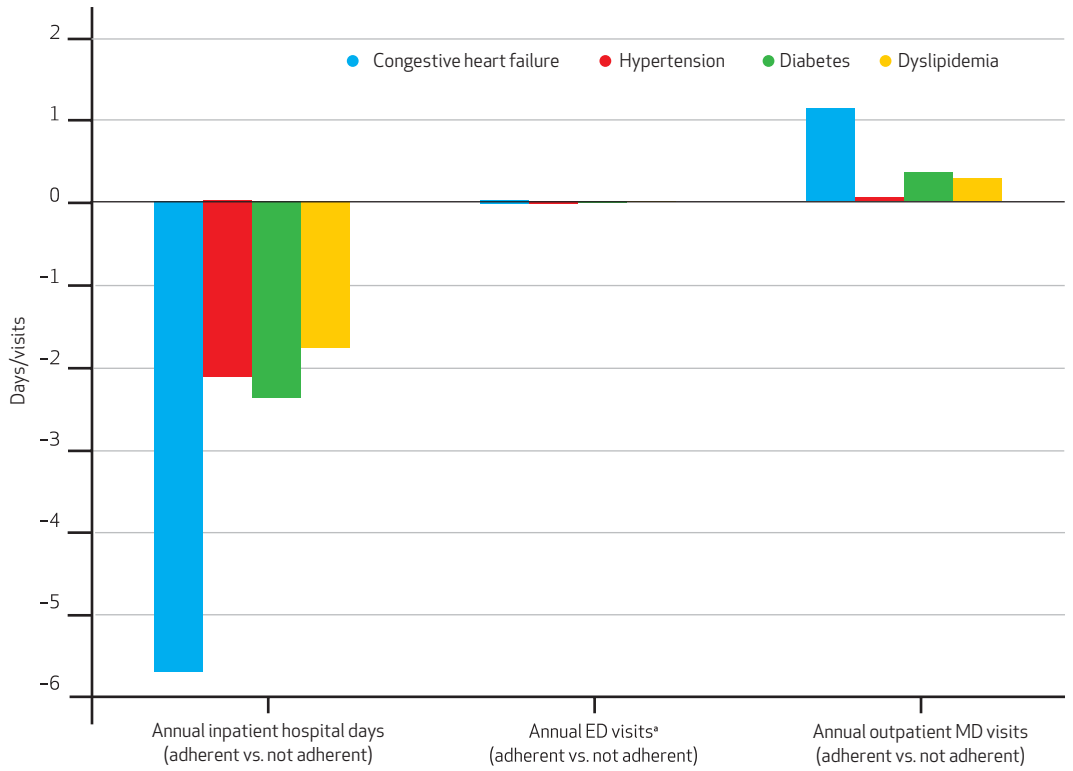
Exhibit 1 presents estimates of the effects of adherence versus nonadherence from the multivariate models of health services use.[24] Across all conditions, adherence was associated with significantly lower annual inpatient hospital days, ranging from 1.18 fewer days for dyslipidemia to 5.72 fewer days for congestive heart failure. Annual emergency department visits were fractionally lower (between 0.01 and 0.04 visits per patient per year) among adherent patients. Finally, adherent patients visited their doctors more often than their nonadherent peers did, with the exception of people with hypertension (not statistically significant).

The effect of adherence on hospitalization was greater (in absolute value) for people age sixty-five and older than for younger patients for all conditions. Adherent patients in the older group had 5.87 (in cases of congestive heart failure), 3.14 (hypertension), 3.41 (diabetes), and 1.88 (dyslipidemia) fewer inpatient hospital days annually (Exhibit 2), compared to 4.74, 0.57, 0.83, and 0.44 fewer days, respectively, for adherent patients in the younger group (data not shown).

Exhibit 3 presents results from the models of health services spending. As we anticipated, adherent patients had higher pharmacy spending than those who were not adherent. The average

EXHIBIT 1

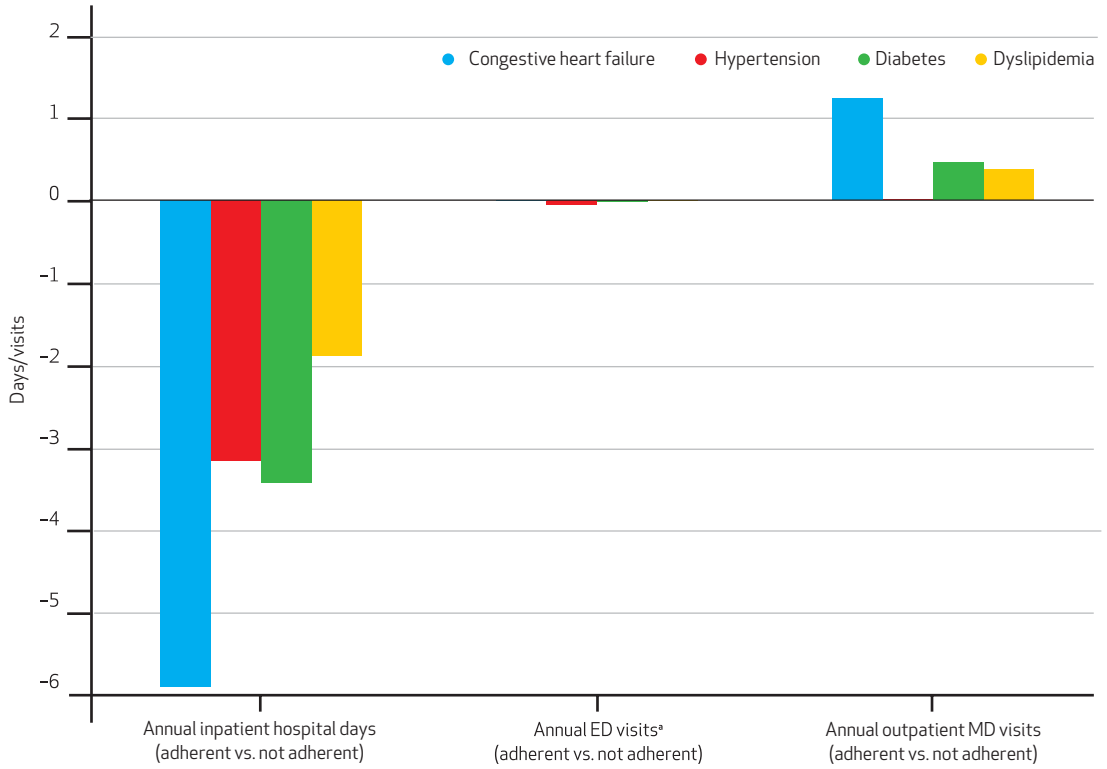
Impact Of Medication Adherence In Chronic Vascular Disease On Health Services Use, 2005–08



SOURCE CVS Caremark integrated pharmacy and medical administrative claims data, January 1, 2005–June 30, 2008. **NOTES** Presented are marginal effect estimates from linear fixed-effects models of health services use. All models included a weighted Charlson Comorbidity Index (see Notes 18–20 in text); two year-indicator variables; dummy variables for age 65 or older, male, and adherent; and interaction terms for adherent with male and age 65 or older. All estimates were significant at $p < 0.01$ except emergency department (ED) visits for congestive heart failure patients ($p < 0.05$) and outpatient physician visits for patients with hypertension (not significant). [a]Values for this segment of the exhibit are as follows. Congestive heart failure: −0.04; hypertension: −0.03; diabetes: −0.02; and dyslipidemia: −0.01.

EXHIBIT 2

Impact Of Medication Adherence In Chronic Vascular Disease On Health Services Use For Patients Age 65 And Older, 2005–08



SOURCE CVS Caremark integrated pharmacy and medical administrative claims data, January 1, 2005–June 30, 2008. **NOTES** Presented are marginal effect estimates from linear fixed-effects models of health services use. All models included a weighted Charlson Comorbidity Index (see Notes 18–20 in text); two year-indicator variables; dummy variables for age 65 or older, male, and adherent; and interaction terms for adherent with male and age 65 or older. All estimates were significant at $p < 0.01$ except emergency department (ED) visits for congestive heart failure patients (not significant), emergency department visits for dyslipidemia patients ($p < 0.10$), and outpatient physician visits for hypertension patients (not significant). [a]Values for this segment of the exhibit are as follows. Congestive heart failure: −0.01; hypertension: −0.05; diabetes: −0.02; and dyslipidemia: −0.01.

annual pharmacy spending of adherent patients was $1,058 more for those with congestive heart failure, with comparable figures of $429 for hypertension, $656 for diabetes, and $601 for dyslipidemia.

In all four conditions, annual medical spending was significantly lower for adherent patients. Adherence reduced average annual medical spending by $8,881 in congestive heart failure, $4,337 in hypertension, $4,413 in diabetes, and $1,860 in dyslipidemia.

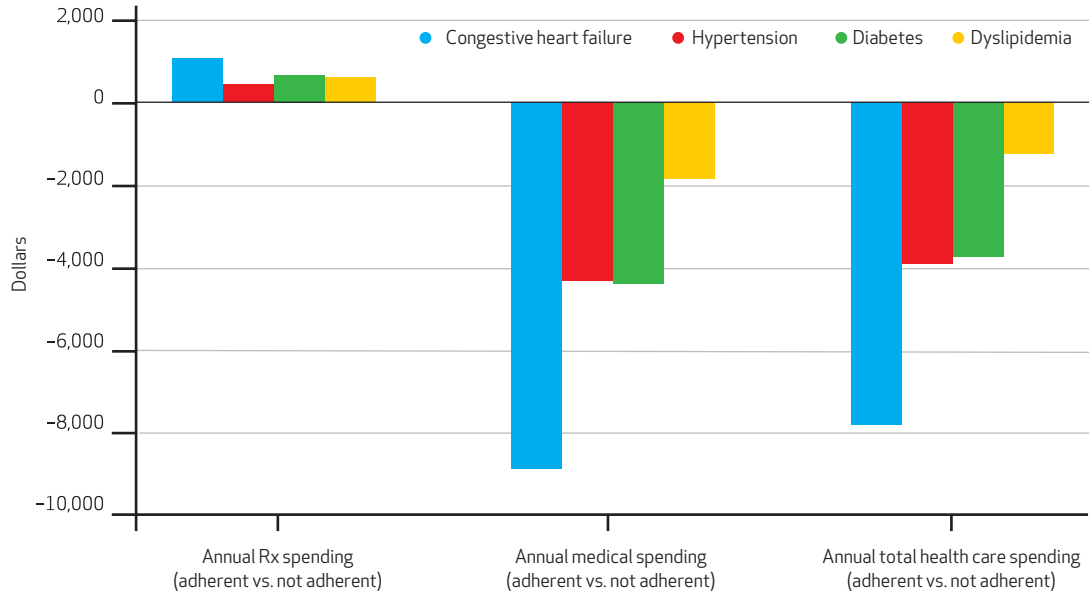
Particularly important from a policy perspective is the impact of medication adherence on total health care spending. Across the board, adherent patients spent significantly less than nonadherent patients. Annual per person savings amounted to $7,823 for congestive heart failure, $3,908 for hypertension, $3,756 for diabetes, and $1,258 for dyslipidemia. Combining the increases in pharmacy spending with the decreases in medical spending, average benefit-cost ratios from adherence for the four vascular conditions we examined were 8.4:1 for congestive heart failure, 10.1:1 for hypertension, 6.7:1 for diabetes, and 3.1:1 for dyslipidemia.

The impact of adherence on total health care spending was similar for patients in both age groups with congestive heart failure, but the effects of adherence in the other three conditions were more pronounced for patients age sixty-five and older. Annual total per person health care savings in the older group were $7,893 for congestive heart failure, $5,824 for hypertension, $5,170 for diabetes, and $1,847 for dyslipidemia (Exhibit 4). Average benefit-cost ratios from adherence for this group were 8.6:1 for congestive heart failure, 13.5:1 for hypertension, 8.6:1 for diabetes, and 3.8:1 for dyslipidemia.

In general, adherence effects did not differ substantially by sex. The exception was in congestive heart failure, where females experienced greater reductions in health services use and

EXHIBIT 3

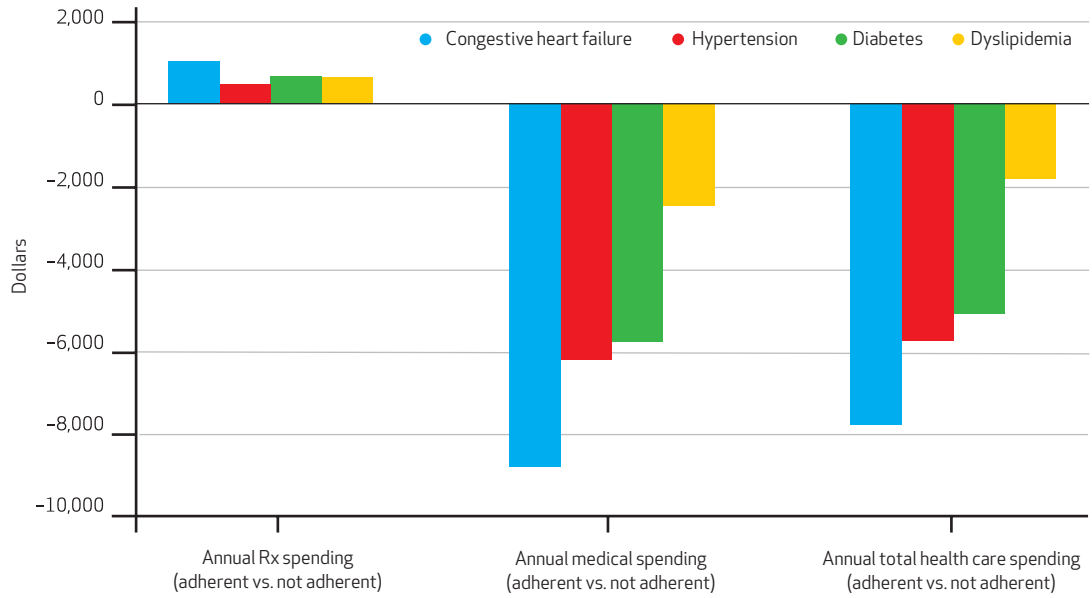
Impact Of Medication Adherence In Chronic Vascular Disease On Health Services Spending, 2005–08



SOURCE CVS Caremark integrated pharmacy and medical administrative claims data, January 1, 2005–June 30, 2008. **NOTES** Presented are marginal effect estimates from linear fixed-effects models of health services cost. All models included a weighted Charlson Comorbidity Index (see Notes 18–20 in text); two year-indicator variables; dummy variables for age 65 or older, male, and adherent; and interaction terms for adherent with male and age 65 or older. All estimates were significant at $p < 0.01$.

EXHIBIT 4

Impact Of Medication Adherence In Chronic Vascular Disease On Health Services Spending For Patients Age 65 And Older, 2005–08



SOURCE CVS Caremark integrated pharmacy and medical administrative claims data, January 1, 2005–June 30, 2008. **NOTES** Presented are marginal effect estimates from linear fixed-effects models of health services cost. All models included a weighted Charlson Comorbidity Index (see Notes 18–20 in text); two year-indicator variables; dummy variables for age 65 or older, male, and adherent; and interaction terms for adherent with male and age 65 or older. All estimates were significant at $p < 0.01$.

spending. All model results are presented in Appendix Tables A5–A11.[17]

Discussion

Our results are evidence that medication adherence reduces total annual health care spending for people with chronic vascular disease. Savings are realized mainly through reduced inpatient hospital days and emergency department visits. Moreover, adherence effects are more pronounced for patients age sixty-five and older.

The issue of medication nonadherence in the elderly was implicitly addressed by the Affordable Care Act of 2010. This legislation progressively reduces, and will eventually close, the existing gap in prescription drug coverage for Medicare beneficiaries (the Part D "doughnut hole"). More generally, the act provides for therapy management and covers certain wellness programs that might improve medication adherence and other aspects of patient compliance with health regimens.[25] Our work suggests that policy makers were prudent in including those provisions in the new law.

Our analysis demonstrates that the additional pharmacy spending incurred from adherence is more than offset by the medical savings realized. The question then becomes whether or not policies and programs that are implemented to improve adherence can do so at costs that do not exceed the expected benefits. Findings from Medicare disease management demonstrations have been mixed: Only 20 percent of evaluated programs have been near or at budget-neutrality.[26]

However, the cost of an adherence intervention is directly related to the mode of delivery. Complex, coordinated care involving physicians, nurses, and case managers may be both successful and costly. Alternatives that require fewer resources—such as electronic monitoring devices and pharmacist-led patient counseling—have shown promise in improving patients' medication adherence at less expense.[27]

To permit rigorous evaluation, policy analysts trained in economics methods should collect data on the costs and benefits of adherence interventions. It is important to note that altering pharmacy benefit designs to improve medication adherence does not necessarily impose additional costs. Value-based insurance designs address cost-related nonadherence by reducing or eliminating patient copayments for medications used to manage chronic conditions. These designs do not add to spending; rather, they shift spending from the enrollee to the plan's sponsor.[28]

Conclusions

In light of the Affordable Care Act's expansion of access to medical care, policy makers must now search for ways to improve health outcomes while reducing spending. Our results indicate that despite higher pharmacy spending, medication adherence by patients with chronic vascular disease provides substantial medical savings, as a result of reductions in hospitalization and emergency department use. Benefit-cost ratios range from 2:1 for adults under age sixty-five with dyslipidemia to more than 13:1 for older patients with hypertension.

Given these findings, plan sponsors, government payers, and patients should consider participating in programs that improve medication adherence, as long as intervention costs do not exceed the estimated health care savings. Value-based insurance design, electronic monitoring devices, and pharmacist-led counseling are among the least costly alternatives. No matter what the intervention, actively encouraging medication adherence for chronic disease should be a top priority. ■

Selected findings from this work were delivered in an oral presentation at the third biennial conference of the American Society of Health Economists at Cornell University, in Ithaca, New York, on June 21, 2010. A related poster presentation was given at the 2010 AcademyHealth Annual Research Meeting, in Boston, Massachusetts, on June 28, 2010. The authors thank participants at those meetings for their interest and suggestions. Invaluable were the critical comments of three anonymous reviewers and the editors. The authors are thankful for those individuals' contribution to this work. The views expressed by the authors do not necessarily represent the views of the Centers for Medicare and Medicaid Services or the US government.

NOTES

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17 To access the Appendix, click on the Appendix link in the box to the right of the article online.

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22 See Appendix Section 2 (see Note 17) for a comparison of our linear fixed-effects models to pooled ordinary least-squares estimation. This exercise largely confirms the endogeneity of adherence and shows that prior studies probably overestimated the absolute value of the impact of adherence on health services use and cost.

23 Fixed-effects modeling does not allow for the control of confounders that vary over time. Thus, for example, if patients who become adherent simultaneously start exercising regularly (assuming that both of these behavioral changes reduce health services use and spending), the estimated impact of adherence would remain biased. Another drawback of the linear fixed-effects modeling approach is that it leaves open the possibility of reverse causality. That is, the reported relationships could indicate an impact of hospitalization on adherence. For example, a hospitalization may shock a patient into becoming adherent. We examined this possibility by estimating the impact of prior adherence on hospitalization and found no effect.

24 Bivariate relationships between adherence and health services use and spending are presented in Appendix Table A4 (see Note 17). The complete set of linear fixed-effects model results are provided in Appendix Tables A5–A10.

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28 Of course, there would certainly be some administrative fixed cost involved in implementing value-based insurance design, and lower copayments might have moral-hazard costs. That is, with low or no out-of-pocket spending required, patients might be induced to fill more prescriptions than necessary, possibly for consumption by other patients with higher copayments.

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Christopher Roebuck and his collaborators at CVS Caremark, the pharmacy health services provider, found themselves well positioned to address a long-standing question: Do people who properly and consistently use medications to manage chronic illness have markedly lower health care spending? "Research kept showing an association," Roebuck says. "Still, investigators couldn't confidently credit adherence for the lower costs." But Roebuck's team had access to integrated medical and pharmaceutical claims data, and expertise in advanced econometric methods—the tools needed to start settling the matter, and to identify the medical services that adherence reduced.

Medication adherence might not be a new issue, Roebuck explains, but it has yet to receive due consideration. Concerns over possible decreased medication use among patients whose high drug spending placed them in the Medicare Part D doughnut hole "heightened interest in adherence and made it part of the reform conversation," he notes. He and his coauthors hope that their current findings will increase the attention focused on adherence, as well as the full clinical and cost-saving potential of pharmacy management.

Roebuck, a health economist, joined CVS Caremark in 2002 and is now its director of health economics and strategic research. He first used the econometric techniques employed in the study reported on here to explore the economics of substance abuse, while he was a senior research associate at the University of Miami School of Medicine. A doctoral candidate in public policy and economics at the University of Maryland Baltimore County, he holds a master of business administration degree in finance from the University of Miami.

Joshua N. Liberman was vice president of strategic research, analytics, and outcomes at CVS Caremark.

Joshua Liberman completed his twenty-year-long affiliation with CVS Caremark in December 2010. As vice president of strategic research, he directed an outcomes research unit with an emphasis on pharmacy benefit designs, prescription drug use patterns, and pharmacy services. Liberman received a master's degree in health science and a doctorate in epidemiology from the Johns Hopkins Bloomberg School of Public Health.

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Troyen A. Brennan is executive vice president and chief medical officer of CVS Caremark.

Troyen Brennan has been executive vice president and chief medical officer of CVS Caremark since 2008. From 2006 to 2008 he was chief medical officer of Aetna. His academic career included appointments as a professor of medicine at Harvard Medical School (1988–2007) and a professor of law and public health at the Harvard School of Public Health (1992–2007). A member of the Institute of Medicine, a diplomate of the American Board of Internal Medicine, and the author of more than 250 original research articles, Brennan holds a master's degree in political economics from Oxford University and a law degree from Yale Law School, as well as a master of public health degree and a medical degree from Yale Medical School.