Overview
Much of the research to date on the effects of medication adherence has focused on health outcomes and medical costs. Analyses of the studies examining the relationship between improved adherence and lower spending have suffered from methodological shortcomings, making findings somewhat controversial. HCFO-funded researcher, Bruce Stuart, Ph.D., University of Maryland at Baltimore, and colleagues designed a medication adherence study with an eye toward addressing prior methodological limitations. Their analyses explored the role of health behaviors in combination with medication adherence to control costs. In their analysis, the researchers concluded that higher medication adherence among diabetic Medicare beneficiaries resulted in lower medical spending.

Background
Diabetes, especially in the elderly, has been linked with a host of comorbidities, including, but not limited to, cardiovascular and kidney disease. However, several clinical trials in the last 10 years have shown positive outcomes in elderly diabetic patients who are prescribed statins and renin-angiotensin-aldosterone system inhibitors (RAAS-Is), which include angiotensin-converting enzyme (ACE) inhibitors, including a delay in onset of certain comorbidities. Consequently, some clinicians support prescribing RAAS-Is or statins to most, if not all, elderly diabetic patients. This increase in prescribing has led researchers to hypothesize that proper adherence to these medications may actually lower health care costs for the patients.

However, the majority of studies that have linked improved adherence with decreased Medicare spending have relied on imperfect methods and failed to substantiate real cost-offsets. For example, some studies have used samples that are not generalizable to the entire Medicare population. Other studies have only looked at a single year of data and are unable to evaluate the longer term benefits of certain drugs, like statins. Additional studies have exhibited survivor bias and reverse causality or “healthy adherer bias.” "Survivor bias” may be

key findings
• Higher adherence to antidiabetic medication over three years for Medicare beneficiaries results in lower Medicare spending.
• Diabetes self-management classes may generate lower Medicare spending.
exhibited in studies that exclude patients who died during the study period. The “healthy adherer bias” has been observed in clinical trials, where patients who were more adherent to a placebo had better health outcomes than patients who were less adherent to a placebo. Therefore, positive outcomes in “good adherers” may not actually be related to a therapeutic benefit of the medication.

Stuart and colleagues sought to address the methodological issues and biases of previous studies. “Our primary aim was to produce valid estimates of potential cost savings from improved medication adherence that policymakers can use to improve the cost effectiveness of the Medicare program,” noted Stuart.

Methods
Stuart and colleagues used data from the Medicare Current Beneficiaries Survey (MCBS) from 1997 through 2005. Randomly selected MCBS respondents complete a baseline survey and are then interviewed every four months for up to three years. They provide personal descriptive information as well as information about their health care costs, utilization, and behavior. Prescription-related information is collected, including prescriptions filled and refilled, name, strength, dose and quantity of doses. The survey does not collect the date the prescriptions are filled nor the number of days’ supply. Every other year, those surveyed are asked specific questions relating to diabetes. The MCBS data is linked with Part A and B claims data to substantiate survey responses.

The final study sample included 3,765 beneficiaries who were surveyed between 1997 and 2002 and had a diagnosis of diabetes at baseline. Diabetes diagnoses were identified through a combination of self-reporting and from claims. From this sample, two overlapping cohorts were created: those who filled prescriptions for a RAAS-I and/or those taking statins. Beneficiaries in these two cohorts were studied until they completed their term in the MCBS, were lost to follow-up, entered a long term care facility, or died. Beneficiaries residing in long-term care facilities or enrolled in a capitated Medicare health plan were excluded from the study sample.

The research team measured adherence using a variation of the medication possession ratio (MPR), calculating the number of pills aggregated into 30-pill fills divided by the total number of months the patient was observed, up to 36 months. This formula for calculating MPR accurately measures drug availability for once-a-day medications such as RAAS-I and statins. Medicare expenditures were calculated using the Medicare Part A and B data, and all dollars were converted to a constant 2006 dollar to control for inflation. The researchers also controlled for many potentially confounding factors including age, sex, race, marital status, education, census region, health status, access to care, and healthy adherer bias.

Using bivariate and multivariate regression analyses, the researchers were able to assess the relationship between a beneficiary’s MPR and their overall Medicare spending.

Results
The two cohorts had very similar baseline characteristics, most likely due to the extensive overlap between the two groups. In fact, 50 percent of RAAS-I users also used statins, and 71 percent of statin users were also prescribed RAAS-I. There were a few baseline differences between the two groups. RAAS-I users were more likely to be a minority, single, and of lower education and socioeconomic status. Statin users were more likely to have high lipid levels.

The median three-year adherence rate was 0.88 for RAAS-I users and 0.77 for statin users. When considering other health behaviors related to diabetes, 41 percent of the total study sample reported taking antidiabetic drugs, and 11 to 12 percent used insulin. More than half of the sample reported a “good understanding of their disease,” checked their blood sugar levels regularly, checked their feet for sores, and attempted to control their diabetes through dietary changes. Participants were less likely to report using exercise, daily aspirin, or a diabetes management class as a mechanism to control their diabetes.

In both the bivariate and multivariate regression analyses, use of RAAS-I and statins were associated with lower Medicare spending. However, the results were more statistically significant in the multivariate regression analysis, and the estimated savings was more profound for statin adherence (a 10 percentage point increase in MPR resulted in an additional savings of $547 for statin users when compared to RAAS-I users).

Very few of the variables designed to detect the “healthy adherer” bias were independently associated with a change in Medicare spending, likely due to the close association among these multiple healthy behaviors. But in combination with medication, for RAAS-I users, exercising and checking feet for sores was associated with lower Medicare spending, while aspirin use yielded higher costs. For statin users, taking a newer antidiabetic agent was associated with lower Medicare spending, but use of a combination of older and newer antidiabetic agents was associated with higher Medicare spending.

The sensitivity tests performed showed that positive changes in MPR are associated with greater cost savings among relatively nonadherent beneficiaries.

In addressing limitations in prior studies on the relationship between medication adherence and spending, the researchers sought to make a contribution to strengthen the knowledge base and help inform policy. Their analysis offered a number of unique contributions to the current literature:

• Rather than consider prescription claims exclusively, the researchers drew on a rich set of information provided through the MCBS.
• Use of the MCBS allowed the researchers to track patterns of the study samples longitudinally for up to three years.
The study included observations for persons who died or were lost to follow-up, allowing for greater generalizability.

Multiple controls addressed potential confounding due to potential survivor and healthy adherer bias.

Results from the study suggest that slightly more than half of beneficiaries taking RAAS-Is and slightly fewer than half of statin users were adherent over three years. The researchers noted that nonadherence may be due to intermittent gaps in compliance or discontinuance of medication. While data limitations did not allow for an analysis of gaps, they were able to track discontinuance rates over time; 15 percent of beneficiaries in the first year and an additional 15 percent by the end of year three ceased medication therapy.

In sum, the researchers found that beneficiaries with better adherence rates had lower spending on Medicare Parts A and B services. For those on statins, a 10 percentage point increase in the medication adherence value was associated with $832 lower Medicare costs, while the same increase in medication adherence for those on RAAS-Is resulted in $285 lower costs. The researchers noted that the potential for savings to the Medicare program is largely concentrated among beneficiaries who are relatively poor adherers to their medication regimen.

The researchers acknowledge that they cannot fully explain the discrepancies between their findings and studies that have gone before, but believe that their analyses address shortcomings in prior studies. They further acknowledge the limitations in their own study, including:

- A lack of service dates and days’ supply, which may have resulted in a slight overestimation of RAAS-Is MPR and understatement of the effects.
- Small sample sizes, limiting their ability to conduct detailed savings analysis.
- A three-year window, which may be insufficient to fully confirm findings associated with a chronic, progressive disease, like diabetes.
- An inability to track beneficiaries who fail to fill prescriptions.
- The lack of Medicare Advantage claims.
- A focus on costs associated with the drugs themselves.

**Policy Discussion**

According to Stuart’s results, improving adherence to RAAS-Is and statins in Medicare beneficiaries with diabetes would result in a reduction in Medicare spending. Furthermore, the sensitivity test results showed that the greatest benefit and savings could be gained by focusing on improving adherence in the “worst adherers.” This information would be helpful to policymakers as they consider the future of Medicare and continue to look for ways to bend the cost curve in health care.

However, perhaps the more important contribution of this study is providing this information to policymakers backed by sound methodology.

“Prior published studies of cost savings from improved medication compliance have generally produced much higher savings estimates than our study, which has led policymakers to be quite skeptical about their validity,” says Stuart. “We wanted to make certain that we avoided any potential bias that would overestimate cost offsets; if anything, our results likely underestimate the potential savings available from improving the medication taking behaviors of Medicare beneficiaries.”

**Conclusion**

Improved adherence to RAAS-Is and statins in Medicare beneficiaries with diabetes is associated with a reduction in overall Medicare spending. Future studies are still needed to analyze whether this cost savings is greater than the potential cost of improving adherence in these populations. However, these results provide promising information to policymakers as they continue to consider how to bend the cost curve of health care in the United States.

**For More Information**

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**About the Author**

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**Endnotes**
