Association of Medication Adherence with Hospital Utilization and Costs Among Elderly with Diabetes Enrolled in a State Pharmaceutical Assistance Program

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ABSTRACT

BACKGROUND: Medication adherence is crucial for the successful treatment among elderly patients with diabetes taking oral antidiabetic medications (OAMs). Cost of medications, lack of insurance coverage, and low income are major contributing factors towards medication nonadherence. State pharmaceutical assistance programs (SPAPs) provide medications at little or no cost to income-eligible patients and have potential to improve medication adherence among elderly patients. Despite this, limited research has focused on the association of medication adherence with health care utilization among elderly patients enrolled in SPAPs, and inclusion of health care costs as an outcome is even rarer.

OBJECTIVE: To evaluate the relationship between adherence to OAMs and hospital utilization and costs among elderly patients with diabetes who were enrolled in a SPAP.

METHODS: This retrospective observational study included elderly patients with diabetes enrolled in Pennsylvania's Pharmaceutical Assistance Contract for the Elderly (PACE) program in 2015. Medication adherence was estimated as the proportion of days covered (PDC; adherent: PDC $\geq$ 80%, nonadherent: PDC < 80%). Hospital utilization and costs were estimated using hospital discharge records from the Pennsylvania Health Care Cost Containment Council. Multiple adjusted regression analyses were used to examine the association of medication adherence with hospital utilization (all-cause and diabetes-related number of inpatient hospital visits and length of stay [LOS]) and costs.

RESULTS: Among 9,497 elderly PACE enrollees with diabetes, 81% were adherent, and 21% were hospitalized. Compared with adherent patients, patients who were nonadherent to OAMs had twice the odds of all-cause and diabetes-related hospitalization. Controlling for covariates, nonadherent patients had 27% more all-cause (95% CI=9%-36%) and 21% more diabetes-related (95% CI=5%-40%) hospital visits than adherent patients. Covariate-adjusted LOS for nonadherent patients was 24% longer than that of adherent patients for all-cause hospitalization (95% CI=1.171-1.311) and 12.7% longer for diabetes-related hospitalization (95% CI=1.036-1.227). Medication nonadherence was associated with significantly greater all-cause (\$22,670 vs. \$16,383; $P<0.0001$) and diabetes-related (\$13,518 vs. \$12,634; $P=0.0003$) hospitalization costs.

CONCLUSIONS: Among SPAP-enrolled elderly patients, nonadherence to OAMs was significantly associated with increased risk of hospitalization, longer hospital stays, and greater hospitalization costs. Attention is needed to improve medication adherence among elderly receiving financial assistance to pay their prescriptions to reduce economic burden on the health care system.

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What is already known about this subject

- Previous research among patients with diabetes supports the link between medication adherence and lower health care utilization and costs.
- Elderly patients find medication adherence challenging for several reasons, but cost of prescription medications is a major barrier to medication adherence.
- State pharmaceutical assistance programs (SPAPs) provide financial assistance to elderly patients for the purchase of prescription medications.

What this study adds

- This study included residence in a pharmacy desert, representing low geographic accessibility to a nearby pharmacy, as one of the predictors, while studying the association of medication adherence with health outcomes.
- Compared with earlier studies of SPAP-enrolled elderly patients with diabetes, different and more health care utilization and costs variables were analyzed, such as all-cause and diabetes-specific number of inpatient visits, length of inpatient stay, and hospitalization costs.
- This study adds new evidence and extends the current literature on medication adherence and health outcomes among elderly SPAP beneficiaries with diabetes.

Diabetes is one of the most prevalent chronic diseases that is responsible for increased mortality and morbidity in the United States.^{1,2} Total cost of the disease in 2017 was estimated to be \$327 billion, including \$237 billion of direct medical costs and \$90 billion due to decreased productivity.³ Prevalence of diabetes increases with age, and as of 2015, 25.2% (about 12 million) of the population who were 65 years and older had diabetes.⁴

The majority of elderly patients with diabetes fail to achieve optimal glycemic control with diet, exercise, and lifestyle changes and require oral antidiabetic medications (OAMs).⁵ Medication adherence is crucial for successful treatment among elderly patients taking OAMs.⁶ Results of higher adherence to OAMs include improved glycemic control, reduced

FIGURE 1 Study Design and Data Sources

^aHad at least 1 prescription fill for an OAM during the 6-month period before the index date.

OAM=oral antidiabetic medication; PACE=Pharmaceutical Assistance Contract for the Elderly; PHC4=Pennsylvania Health Care Cost Containment Council; Rx=prescription.

diabetes-related complications, improved quality of life, lower risk of premature death, fewer emergency department visits, fewer hospitalizations, and reduced medical costs.⁷⁻¹⁰ Despite the importance of medication adherence, nonadherence to OAMs represents a substantial problem in the United States, with medication adherence rates ranging from 36% to 59% among elderly patients with diabetes.^{11,12} In 2007, the Centers for Medicare & Medicaid Services (CMS) developed a star ratings system to evaluate the performance of Medicare Advantage and Prescription Drug (Part D) plans, and adherence to diabetes medications is one of the metrics used to calculate the star rating.¹³⁻¹⁵ Medicare plan sponsors use star ratings to qualify for quality bonus payments, to maintain or increase beneficiary enrollment, and to avoid termination by CMS.¹⁶ Hence, adherence to OAMs is a matter of great importance to all stakeholders—patients, health care providers, policymakers, and insurance plan sponsors.

There are several reasons why elderly patients do not follow their prescriptions.^{17,18} The cost of medications has been identified as a major contributing factor to medication nonadherence.^{19,20} Approximately 1 in 10 adults and 4.4% of elderly patients in the United States do not consume medications as prescribed because they cannot afford it.²¹ Patients with low income and limited or no prescription drug coverage are more likely to be nonadherent because of the cost burden.^{22,23} State pharmaceutical assistance programs (SPAPs) provide medications at little or no cost to income-eligible patients. Nearly all U.S. individuals aged 65 years and older are enrolled in Medicare. However, Medicare Part B does not pay for outpatient medications. In addition, not all elderly individuals are eligible for Medicaid, which provides prescription coverage. Consequently, SPAPs were implemented to help non-Medicaid low-income elderly patients.²⁴ Since Medicare Part D was

implemented in 2006, the role of many SPAPs has evolved to provide benefits that are coordinated with Part D prescription coverage.

Although there is growing evidence that medication adherence helps to improve health outcomes and reduce health care costs,²⁵⁻³¹ limited research has focused on the association between medication adherence and health care utilization among elderly SPAP enrollees, and inclusion of health care costs as an outcome is even rarer.³² Hence, the objective of this study was to evaluate the relationship of medication adherence to hospital utilization and costs among elderly patients enrolled in a SPAP.

Methods

Study Design and Data Sources

A retrospective observational study using electronic databases for elderly patients enrolled in a Pennsylvania SPAP was conducted (Figure 1). This study used data from January 1, 2015, through December 31, 2016, the most recent data available at the time of analysis. The databases consisted of (a) cardholder data and prescription claims data from the Pharmaceutical Assistance Contract for the Elderly (PACE) program and (b) The Pennsylvania Health Care Cost Containment Council's (PHC4) hospital discharge data, which were linked to PACE data. PACE is a SPAP that provides low-cost prescription medications to more than 250,000 income-eligible Pennsylvania residents aged 65 years or older. During the study period, PACE's income limits were \$23,500 for single individuals and \$31,500 for married persons. PHC4 is an independent state agency that collects, analyzes, and disseminates hospital data in order to improve health care for Pennsylvanians. PHC4 collects data on more than 1.7 million inpatient discharges from Pennsylvania hospitals each year.^{33,34}

Data on patient characteristics and dispensed prescriptions were obtained from PACE's cardholder and pharmacy claims files. Prescription data provided by PACE included claims paid directly by PACE, as well as supplemental prescription drug event data from Medicare Part D plans partnering with PACE to provide integrated Part D and SPAP benefits. Information on hospitalizations, length of stay, and associated costs were extracted from the PHC4 hospital discharge database. This study was approved by the Institutional Review Board of the University of the Sciences in Philadelphia.

The index date for each eligible patient was defined as the first prescription fill date for an OAM in 2015. Medication adherence, hospital utilization, and costs were evaluated during a fixed 12-month observation period including and following the index date. Because previous research suggests that medication adherence may be higher during the initial treatment period than during ongoing treatment, this study adopted a prevalent user approach.^{35,36} With this approach, only established users (defined as patients who had at least 1 fill for an OAM during the 6-month period preceding their 2015 index date) were included.

Study Population

Individuals who met the following criteria were included in this study:

- Had at least 12 months of continuous enrollment in PACE between their index fill dates and December 31, 2016.
- Were alive throughout the 12-month post-index observation period.
- Were either not enrolled in Medicare Part D or had Part D coverage with a Medicare Part D plan partnering with PACE. Individuals with Part D coverage through nonpartner plans were excluded, which ensured that a complete record of all prescriptions paid for by either PACE or Part D was available for analysis.
- Had at least 2 prescription claims for OAMs in 2015. Although we were unable to verify a diagnosis of diabetes because of the lack of health care data before PACE enrollment, patients meeting the study's OAM prescription criteria would generally be expected to receive long-term treatment for diabetes.

Because methods used for calculating adherence for nonoral and oral medications differ,^{37,38} adherence measurements of patients using non-OAMs may not be directly comparable with those of patients using only OAMs. Therefore, patients using non-OAMs with or without OAMs were excluded.

A pharmacy desert represents low geographic accessibility to a nearby community pharmacy, which may create disparities across communities in access to prescription medications and thereby medication adherence.³⁹ To control for potential pharmacy desert effects, a dichotomous measure of residence

within a pharmacy desert was included as a covariate. Because pharmacy desert status is based on the distance between a patient's residence and a nearby pharmacy,³⁹ which assumes that individuals obtain prescriptions as walk-in patients, individuals who had any mail-order prescription claims were excluded. Similarly, individuals who resided in nursing homes or other long-term care settings during the observation period were excluded. Since this study was evaluated from a payer's perspective, patients whose hospitalizations during the observation period were paid for by non-Medicare payers were also excluded.

Medication Adherence Measurement

Adherence to OAMs was calculated as the proportion of days covered (PDC) using prescription claims data. PDC is a widely used and well-accepted standard measure to evaluate medication adherence in various diseases and is the adherence measure preferred by the Pharmacy Quality Alliance (PQA).^{37,40,41} PDC was defined as the percentage of days during the 12-month post-index observation period that the patient had at least 1 OAM available.⁴² The formula used to calculate PDC is illustrated by the following equation:

$$\text{PDC} = (\text{Number of days in the 12-month post-index observation period when at least 1 OAM was available} \div 365) \times 100$$

The "at least 1" definition of PDC takes into account overlapping prescriptions, changes in therapeutic regimen, and use of concurrent medications. This measurement strategy is recommended by PQA and has been widely used by other researchers.^{41,43-45} Patients were categorized as "adherent" if PDC was $\geq 80\%$ and "nonadherent" if PDC was $< 80\%$, consistent with the dichotomization of medication adherence used in previous studies.^{27,46-49} This dichotomous adherence measure was used as the primary predictor variable in the multivariable analyses.

Health Care Utilization and Costs Measures

The primary outcome evaluated to measure hospital utilization was *risk of hospitalization* (whether a patient had 1 or more inpatient hospitalizations) during the 12-month post-index observation period. Secondary utilization measures included the *number of hospital visits* and *length of stay* (LOS) in days associated with inpatient hospitalization during the 12-month post-index observation period. While calculating these measures, 2 types of inpatient hospitalizations were considered: all-cause and diabetes-related. All-cause hospitalization was defined as an inpatient hospitalization for any reason. Diabetes-related hospitalization was defined as an inpatient hospitalization with *International Classification of Diseases, Ninth Revision, Clinical Modification* codes (250.X0 and 250.X2, X=0-9) or *International Classification of Diseases, Tenth Revision, Clinical Modification* codes (E11 and E13) and with diagnosis

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TABLE 1 Patient Characteristics by Adherence Status^a (N = 9,497)

Characteristics	Adherent (PDC ≥ 80%) (n = 7,696)		Nonadherent (PDC < 80%) (n = 1,801)		P Value ^b
	N or mean	% or SD	N or mean	% or SD	
Age, years (mean and SD)	79.82	6.83	79.85	7.10	0.8659
Sex					
Male	2,105	27.35	516	28.65	0.2670
Female	5,591	72.65	1,285	71.35	
Race					
White	6,989	90.81	1,541	85.56	<0.0001
African American	305	3.96	117	6.50	
Other	81	1.05	28	1.55	
Unknown	321	4.17	115	6.39	
Ethnicity					
Hispanic	100	1.30	41	2.28	0.0020
Non-Hispanic	7,596	98.70	1,760	97.72	
Annual income, 2014 U.S. dollars					
< \$5,000	108	1.40	37	2.05	0.3145
\$5,000-\$9,999	552	7.17	125	6.94	
\$10,000-\$14,999	2,367	30.76	567	31.48	
\$15,000-\$19,999	2,532	32.90	579	32.15	
≥ \$20,000	2,137	27.77	493	27.37	
Marital status					
Single/widowed	4,996	64.92	1,144	63.52	0.2956
Married	1,811	23.53	461	25.60	
Divorced	716	9.30	156	8.66	
Married but living separately	173	2.25	40	2.22	
Lived in a pharmacy desert					
Yes	3,559	46.24	785	43.59	0.1225
No	3,935	51.13	968	53.75	
Total number of unique medications ^c (mean and SD)	10.53	4.54	10.26	4.96	0.0327
OPP (mean and SD)	8.12	10.13	7.39	11.03	0.0099
Medication adherence					
PDC (mean and SD)	94.87	5.15	58.74	17.24	<0.0001
PDC (median and IOR)	96.00	7.00	64.00	24.00	

^aDifferences in continuous variables were examined using t-tests, and differences in categorical variables were examined using chi-square tests.

^bStatistically significant if P < 0.05.

^cTotal number of unique medications based on unique classes of medications on hand for any disease during the 12-month post-index observation period for a patient. HIC3 classification was used to determine class of the medication.

HIC3 = Hierarchical Ingredient Code Level 3; IQR = interquartile range; OPP = out-of-pocket payment; PDC = proportion of days covered; SD = standard deviation.

codes reflecting diabetes-related complications, which was adapted from the American Diabetes Association's study of U.S. economic costs of diabetes.³

Hospitalization cost included only direct medical costs related to inpatient hospitalization, since this study adopted a third-party payer (Medicare) perspective. Direct nonmedical and indirect medical costs were not included. Direct inpatient hospitalization cost was the sum of room and board costs, ancillary costs, drug costs, equipment costs, specialty costs, miscellaneous costs, and professional fees. Costs were calculated from total charges using hospital-level, Medicare-specific, cost-to-charge ratios for the year of hospitalization (2015 or

2016). All costs were converted to 2015 U.S. dollars using the medical component of the Consumer Price Index. Costs were calculated separately for all-cause and diabetes-related hospitalizations.

Covariates or Other Variables

Patient-level sociodemographic measures, including age, sex, race, ethnicity, annual income, and marital status, were obtained from PACE's cardholder database. Patients were categorized as residing in a pharmacy desert or not, using the classification of pharmacy deserts developed in an earlier study.⁵⁰ The total number of unique medications based on First

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TABLE 2 Unadjusted Health Care Utilization and Costs Among the Study Population During the 12-Month Post-Index Observation Period, Overall and by Adherence Status^a (N=9,497)

Health Care Utilization/Cost Variable	All (N=9,497)	Adherent (PDC ≥80%) (n = 7,696)	Nonadherent (PDC <80%) (n = 1,801)	P Value ^b
Number of inpatient hospital visits per 100 persons (SD)				
All-cause	34 (0.83)	29 (0.73)	54 (1.14)	<0.0001
Diabetes-related	10 (0.40)	9 (0.37)	15 (0.50)	<0.0001
Length of stay in days, mean (SD)				
All-cause	1.80 (5.82)	1.45 (4.78)	3.31 (8.85)	<0.0001
Diabetes-related	0.43 (2.14)	0.36 (1.89)	0.71 (2.97)	<0.0001
Costs of inpatient hospitalizations, mean (SD)^c				
All-cause	\$3,767 (\$12,342)	\$3,077 (\$10,250)	\$6,716 (\$18,538)	<0.0001
Diabetes-related	\$965 (\$5,073)	\$847 (\$4,683)	\$1,468 (\$6,455)	0.0001

^aDifferences between adherent and nonadherent patients were examined using t-tests.

^bStatistically significant if $P < 0.05$.

^cPresented in 2015 U.S. dollars.

PDC=proportion of days covered; SD=standard deviation.

DataBank's Hierarchical Ingredient Code Level 3 classification filled during the 12-month post-index observation period (regardless of whether they were used to treat diabetes) was used as a proxy measure for disease burden.^{27,46,49,51} For each patient, the out-of-pocket payment per OAM prescription was calculated by dividing the sum of all PACE copayments, Part D premiums collected by PACE against drug cost at the point of sale, and patient pay amounts (for Part D claims that were not also submitted to PACE) by the total number of OAM prescriptions filled during the 12-month post-index observation period.

Statistical Analysis

Descriptive statistics for the study sample were reported. For unadjusted analyses, Student's t-tests for continuous variables and chi-square tests for categorical variables were used to compare the adherent and nonadherent groups. Multivariable logistic regression was used to evaluate the association between medication adherence and hospitalization, while adjusting for sociodemographic characteristics, pharmacy desert residence, number of unique medications, and out-of-pocket payment. Odds ratios and 95% confidence intervals (CIs) were reported.

The relationship between medication adherence and hospital utilization (number of hospital visits and LOS) was evaluated using separate covariate-adjusted zero-inflated negative binomial regression (ZINB) analyses. ZINB regression analysis is appropriate when count data (e.g., number of hospital visits and LOS) show a very skewed distribution and overdispersion and exhibit many zero count observations.⁵² Comparison of the ZINB and negative binomial models was performed using the Vuong test, which indicated that the ZINB model exhibited a significantly better fit to the data. Incidence rate ratios (IRRs) and 95% CIs were reported for ZINB models. The IRR

represents the rate of hospital utilization during the observation period in nonadherent compared with adherent patients.

Two-part models were used to examine the association of medication adherence with hospitalization costs⁵³; the first part captured the probability of an all-cause or diabetes-related inpatient hospitalization, and the second part used general linear models with a gamma distribution and log link function to estimate costs, while controlling for covariates. Predicted cost estimates and corresponding 95% CIs based on generalized linear models, and corresponding *P* values based on t-tests, were reported.

All statistical analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

Study Population

Overall, 81% of patients were adherent (n=7,696), and 19% of patients were identified as nonadherent (n=1,801; Table 1). Adherent patients were more likely to be White (90.81% vs. 85.56%; $P < 0.0001$) and non-Hispanic (98.70% vs. 97.72%; $P = 0.0020$) compared with nonadherent patients. Adherent patients filled prescriptions for more unique medications (10.53 vs. 10.26; $P = 0.0327$), paid higher out-of-pocket payments (\$8.12 vs. \$7.39; $P = 0.0099$), and had greater average PDC (95% vs. 59%) compared with nonadherent patients. No significant differences were observed between adherent and nonadherent patients for age, sex, annual income, marital status, and pharmacy desert status.

Unadjusted Health Care Utilization and Costs

A significantly greater proportion of nonadherent patients had at least 1 all-cause (29% vs. 18.8%; $P < 0.0001$) or diabetes-related (10.7% vs. 6.7%; $P < 0.0001$) inpatient hospitalization during

TABLE 3 Multivariable Regression Analyses Results Determining Relationship Between Medication Adherence with Risk of Hospitalization and Health Care Utilization Among Elderly Who Were Enrolled in a SPAP (N= 9,497)

Type of Inpatient Hospital Visit	Risk of Hospitalization		Hospital Visits		LOS (in days)	
	Adjusted OR ^a	95% CI	Adjusted IRR ^b	95% CI	Adjusted IRR ^b	95% CI
All-cause	2.020	1.776-2.297	1.2676	1.1894-1.3510	1.2393	1.1713-1.3112
Diabetes-related	1.750	1.455-2.103	1.2012	1.0404-1.3869	1.1280	1.0369-1.2271

Note: Adjusted for predefined covariates: age, sex, race, ethnicity, income, marital status, pharmacy desert, number of unique medications, and out-of-pocket payments.

^aOdds ratio for nonadherence versus adherence.

^bIncidence rate ratio for nonadherence versus adherence.

CI= confidence interval; LOS=length of stay; SPAP= state pharmaceutical assistance program.

the observation period than adherent patients (Appendix A, available in online article). The number of inpatient hospital visits per 100 persons was 34 for all-cause and 10 for diabetes-related admissions (Table 2). The average LOS for hospitalized patients was nearly 2 days for all-cause hospitalization and approximately one-half day for diabetes-related complications. Average annual inpatient costs for all-cause and diabetes-related hospitalizations were \$3,767 and \$965, respectively.

Table 2 also shows hospital utilization and costs by adherence status. Adherent patients had significantly fewer all-cause (29 vs. 54; $P<0.0001$) and diabetes-related (9 vs. 15; $P<0.0001$) inpatient hospital visits compared with nonadherent patients. Similarly, adherent patients had significantly shorter LOS for all-cause (1.45 vs. 3.31; $P<0.0001$) and diabetes-related (0.36 vs. 0.71; $P<0.0001$) hospitalizations than nonadherent patients. Inpatient cost was significantly higher for nonadherent patients than for adherent patients (mean \$6,716 vs. \$3,077; $P<0.0001$). Similarly, nonadherent patients had significantly higher diabetes-related hospitalization cost than adherent patients (mean \$1,468 vs. \$847; $P=0.0001$).

Among patients who had at least 1 inpatient hospital admission during the 12-month post-index observation period, the number of admissions per 100 persons was 164 for all-cause hospitalization and 48 for diabetes-related hospitalization (Appendix B, available in online article). Average LOS among hospitalized patients was 9 days for all-cause hospitalizations and 2 days for diabetes-related hospitalizations. Hospitalized patients incurred average costs of \$18,066 and \$4,623 for all-cause and diabetes-related hospitalizations, respectively. The number of all-cause hospitalizations per 100 persons was significantly lower for adherent patients than for nonadherent patients (156 vs. 188; $P<0.0001$). However, the difference in number of diabetes-related hospitalizations per 100 persons between adherent and nonadherent patients was not statistically significant (47 vs. 51; $P=0.2518$). The annual average LOS for all causes was significantly lower for adherent patients than nonadherent patients (7.70 vs. 11.41; $P<0.0001$). Similarly,

average LOS for diabetes-related hospitalizations was significantly shorter for adherent patients compared with nonadherent patients (1.91 vs. 2.47; $P=0.0254$). Among hospitalized patients, significantly greater all-cause hospitalization cost was observed in nonadherent patients compared with adherent patients (mean \$23,059 vs. \$16,266; $P<0.0001$). However, no significant difference was observed for diabetes-related hospitalization costs among adherent and nonadherent hospitalized patients ($P=0.3179$).

Relationship of Medication Adherence with Hospital Utilization

Regression analyses suggested a negative association between adherence and likelihood of hospitalization (Table 3). When adjusted for predefined covariates, the odds of being hospitalized for all-cause and diabetes-related complications were 2.020 (95% CI=1.776-2.297; $P<0.0001$) and 1.750 (95% CI=1.455-2.103; $P<0.0001$), respectively, for nonadherent patients compared with adherent patients. Nonadherent patients also had significantly greater hospital utilization than adherent patients, when adjusted for baseline characteristics. Controlling for covariates, nonadherent patients had 27% more all-cause (IRR=1.2676; 95% CI=1.1894-1.3510; $P<0.0001$) and 20% more diabetes-related (IRR=1.2012; 95% CI=1.0404-1.3869; $P=0.0124$) hospital visits than adherent patients. Compared with adherent patients, covariate-adjusted LOS for nonadherent patients was 24.0% longer for all-cause (IRR=1.2393; 95% CI=1.1713-1.3112; $P<0.0001$) and 12.8% longer for diabetes-related (IRR=1.1280; 95% CI=1.0369-1.2271; $P=0.0051$) hospitalizations.

Association of Medication Adherence with Hospitalization Costs

When the association between adherence to OAMs and hospitalization costs among subjects who were hospitalized at least once during the observation period was analyzed, while adjusting for covariates, the predicted inpatient hospitalization cost was significantly lower for adherent than for nonadherent

patients for all-cause (\$16,374 vs. \$22,697; $P < 0.0001$) and diabetes-related hospitalization (\$12,659 vs. \$13,515; $P = 0.0039$; Figure 2). These findings indicate that adherence was associated with significant reductions in health care costs.

Discussion

This study aimed to provide real-world evidence of the relationship of adherence to OAMs with inpatient hospital utilization and costs among the elderly enrolled in a SPAP. Compared with adherent patients, those who were nonadherent to OAMs had approximately twice the odds of all-cause and diabetes-related hospitalizations. Nonadherent patients also had significantly more inpatient hospital visits and longer LOS than adherent patients. A negative relationship between medication adherence and health care utilization was observed for all-cause and diabetes-related inpatient hospitalizations. Among the elderly with at least 1 hospitalization, patients who were adherent to OAMs had lower all-cause and diabetes-related inpatient hospitalization costs than nonadherent patients. Adherence-based reductions in hospitalization costs appeared to be driven primarily by lower hospitalization rates among adherent patients.

These findings are consistent with earlier literature indicating that medication nonadherence is associated with greater risk of hospitalization, greater health care utilization, and higher health care costs.^{6,26,27,29,30,54-60} Lau et al. (2004) and Ho et al. (2008) reported that the odds of being hospitalized were 2.53 and 1.58, respectively, for nonadherent patients compared with patients adherent to OAMs.^{54,61} Curtis et al. (2017) demonstrated that among type 2 diabetes patients, nonadherent individuals (PDC < 80%) were significantly more likely to be hospitalized (22.71% vs. 17.65%), had significantly more hospitalizations (mean 0.40 vs. 0.27), and had longer LOS (mean 2.16 vs. 1.25 days) compared with adherent individuals (PDC ≥ 80%).⁵⁵ Roebuck et al. (2011) reported average annual medical savings of \$4,413 due to adherence among patients with diabetes.⁵⁶

Very few studies have reported the linkage of medication adherence with health care utilization and costs among elderly SPAP participants.³² A 2010 study of PACE cardholders by Ding found that adherence across multiple medication classes, including OAM, was associated with lower hospital utilization.³² That study, however, only examined all-cause hospitalization and used a different methodological approach by evaluating the effect of PDC separately for persistent and nonpersistent medication users. In addition, the study did not consider out-of-pocket drug costs or pharmacy desert residence. Hence, the present study adds new evidence and extends the current literature on medication adherence and health care utilization and costs among elderly SPAP beneficiaries with diabetes.

The finding that OAM adherence is associated with significantly lower hospital utilization and cost has important

FIGURE 2 Covariate-Adjusted Inpatient Hospitalization Costs^a Among Users of Service by Adherence Status

	All-Cause (n = 1,907)	Diabetes-Related (n = 708)
Adherent, mean (95% CI)	\$16,374 (\$16,176-\$16,571)	\$12,659 (\$12,348-\$12,970)
Nonadherent, mean (95% CI)	\$22,697 (\$22,220-\$23,173)	\$13,515 (\$13,060-\$13,969)

^aPredicted costs estimates and corresponding 95% CIs based on generalized linear models, and corresponding P values based on paired t-tests.

^b $P < 0.01$.

CI = confidence interval; PDC = proportion of days covered.

implications for federal and state policymakers seeking to reduce health care costs. To realize the potential health care savings that may result from better medication adherence, policy solutions aimed at improving adherence are needed. Our findings emphasize the importance of increasing awareness about medication adherence and the need for earlier identification of poor adherence among SPAP-enrolled patients. Several existing policy efforts that may help to improve medication adherence are based on cost-related considerations, including efforts to increase the availability of cheaper alternative medications, expand insurance coverage, and increase access to prescription assistance programs such as PACE. Expanding access to SPAPs may provide benefits beyond states' direct cost sharing. For example, PACE facilitates enrollees' access to Medicare Part D and the Part D low-income subsidy. These coordinated benefits are reflected in the out-of-pocket costs analyzed in this study.

In addition to these considerations, future policy efforts should also focus on the role that SPAPs, pharmacists, and clinicians can have in educating patients about their health conditions and value of their drug therapy and in

motivating behavioral changes to enhance medication adherence. Policymakers may encourage primary care providers and pharmacies to invest in adherence-enhancing resources, such as counseling services, through financial rewards. Pharmacist-led patient counseling has been shown to increase medication adherence at less expense than the savings generated.⁵⁶ Clinicians and pharmacists may also conduct routine assessments of medication nonadherence in elderly patients enrolled in a SPAP for the early identification of high-risk individuals. Such patients can be targeted with adherence-improving interventions.

Limitations and Strengths

This study has some limitations. First, this study was observational, so definite conclusions about causal relationships between adherence and hospital utilization and costs cannot be established. Second, this study examined the concurrent relationship between medication adherence and hospitalization outcomes during a 12-month post-index observation period. This approach cannot capture variations in adherence that may have altered the outcome at a different time.

Third, the study used a prevalent user design by including only established OAM users. Prevalent users may introduce spillover effects of prestudy adherence on outcomes measured during the study period. The prevalent user sample may have preferentially included patients who have been successful taking OAMs, thereby introducing a “healthy adherer” bias.⁶² Healthy adherer bias could also occur if OAM-adherent patients were more likely than nonadherent patients to have other healthy lifestyle behaviors. In addition, if OAM-adherent patients were similarly adherent to medications for other health conditions, then the positive outcomes associated with OAM adherence may be partially attributable to adherence to other medications. Controlling for healthy adherer effects was beyond the scope of this study.

Fourth, this study measured disease burden based on unique medications used during the observation period when medication adherence and outcomes were measured but did not include a baseline comorbidity measure. Future studies may consider comorbidity measurements in the period before the index fill date to estimate baseline disease burden.

Fifth, elderly patients who used insulin or other injections were excluded to avoid differences in the calculation of medication adherence. Insulin and other injections may be associated with greater disease severity. Hence, this study's findings may not be generalizable to all patients with diabetes. Further research is warranted to understand differences between insulin users and other OAMs users.

Sixth, the strategy of calculating PDC by evaluating whether “at least 1” OAM was available on a given day, while considered the optimal approach to PDC calculation,⁴¹ may overestimate adherence among patients prescribed multiple OAMs who must take all of the medications daily for a therapeutic

benefit.⁴² In addition, claims-based adherence measures such as PDC may not reflect actual medication consumption. Claims data on hospitalizations often do not include information on inpatient medication use, so patients were assumed to be fully adherent to medications during inpatient hospitalizations. It is possible that patients received their daily medications while they were hospitalized, which may have delayed the filling of their prescriptions at a pharmacy.

Previous literature has shown that, on average, different approaches to handling hospitalizations yield adherence estimates that are similar to estimates that incorporate inpatient medication use, and adjustments to PDC are primarily required if patients were hospitalized for >28 days.⁶³ In this study, only 15 of 9,497 patients were hospitalized for >28 days, hence, accounting for inpatient days would be expected to have minimal effect on the final PDC.

Finally, because of unavailability of data, this study could not identify additional assistance such as medication samples from physicians, which may have further reduced costs for patients.

Despite these limitations, this study has unique attributes and offers several important strengths. The study used a statewide comprehensive dataset of linked prescription and hospitalization records and reported noteworthy findings for SPAP-enrolled elderly patients with diabetes in a real-world setting. Medicare is the largest payer of health care in the United States, but it is facing decreased funding; therefore, understanding the factors associated with high risk and high users of Medicare-reimbursed services is critical.

This study is valuable in that it provides new evidence about high-risk elderly patients with diabetes who have higher hospital utilization and Medicare-covered costs. Additionally, the methodological approach of this study, which is based on the linkage of low-cost administrative databases, can be applied to other disease conditions and to other SPAPs to evaluate health outcomes and their economic burden on the U.S. health care system.

Conclusions

The results of this study indicated that, among elderly patients with diabetes who were enrolled in a SPAP, medication nonadherence was significantly associated with an increased risk of hospitalization, greater number of hospital visits, and longer hospital LOS. Consistent with these findings, nonadherence to OAMs was also associated with substantial hospitalization costs among hospitalized SPAP-enrolled elderly patients. These findings suggest that adherence to OAMs among older SPAP-enrolled adults with diabetes may lead to significant benefits for patients without increasing health care resource use and Medicare costs. Application of adherence-enhancing interventions, as well as motivating and monitoring SPAP enrollees for medication adherence, should be a priority for SPAP administrators, particularly when value-based care is changing the health care landscape.

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DISCLOSURES

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APPENDIX A

Proportion of Patients Who Had at Least 1 Hospital Visit During the 12-Month Post-Index Observation Period, Overall and by Adherence Status (N = 9,497)

^aStatistically significant ($P < 0.05$).

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APPENDIX B

Unadjusted Health Care Utilization and Costs Among Patients Who Had at Least 1 Hospital Visit During the 12-Month Post-Index Observation Period, Overall and by Adherence Status^a (N = 1,970)

Health Care Utilization/Cost Variable	All (N = 1,970)		Adherent (PDC ≥ 80%) (n = 1,448)		Nonadherent (PDC < 80%) (n = 522)		P Value ^b
Number of inpatient hospital visits per 100 persons (SD)							
All-cause	164	(1.10)	156	(0.94)	188	(1.42)	<0.0001
Diabetes-related	48	(0.76)	47	(0.74)	51	(0.82)	0.2518
Length of stay in days, mean (SD)							
All-cause	8.68	(10.18)	7.70	(8.56)	11.41	(13.34)	<0.0001
Diabetes-related	2.06	(4.33)	1.91	(4.01)	2.47	(5.11)	0.0254
Costs of inpatient hospitalizations, mean (SD) ^c							
All-cause	\$18,066	(\$21,611)	\$16,266	(\$18,323)	\$23,059	(\$28,260)	<0.0001
Diabetes-related	\$4,623	(\$10,262)	\$4,477	(\$9,933)	\$5,029	(\$11,124)	0.3179

^aDifferences between adherent and nonadherent patients were examined using *t*-tests.

^bStatistically significant if *P* < 0.05.

^cPresented in 2015 U.S. dollars.

PDC = proportion of days covered; SD = standard deviation.