


Hypertension, cholesterol and diabetes medication adherence, health care utilization and expenditure in a Medicare Supplemental sample

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Abstract

Limited evidence exists regarding the relationships between adherence, as defined in Pharmacy Quality Alliance (PQA) medication adherence measures, health care utilization, and economic outcomes. PQA adherence measures for hypertension, cholesterol, and diabetes are of particular interest given their use in Medicare Star Ratings to evaluate health plan performance.

The objective of this study was to assess the relationship between adherence and utilization and cost among Medicare Supplemental beneficiaries included in the aforementioned PQA measures over a 1-year period.

Retrospective cohort study.

Three cohorts (hypertension, cholesterol, and diabetes) of eligible individuals from the Truven Health MarketScan Commercial Claims and Encounters Research Databases (2009–2015) were used to assess associations between adherence and health care expenditure and utilization for Medicare Supplemental beneficiaries.

Generalized linear models with log link and negative binomial (utilization) or gamma (expenditure) distributions assessed relationships between adherence ($\geq 80\%$ proportion of days covered) and health care utilization and expenditure (in 2015 US dollars) while adjusting for confounding variables. Beta coefficients were used to compute cost ratios and rate ratios.

Adherence for all 3 disease cohorts was associated with lower outpatient and inpatient visits. During the 1-year study period, adherence was associated with lower outpatient, inpatient, and total expenditures across the cohorts, ranging from 9% lower outpatient costs (diabetes cohort) to 41.9% lower inpatient costs (hypertension cohort). Savings of up to \$324.53 per member per month in total expenditure were observed for the hypertension cohort.

Our findings indicate adherence is associated with lower health care utilization and expenditures within 1 year.

Abbreviations: CI = confidence interval, CR = cost ratio, GLM = generalized linear models, PDC = proportion of days covered, PMPM = per member per month, PQA = Pharmacy Quality Alliance, RAS = Renin angiotensin system, RR = rate ratio, SD = standard deviation, US = United States.

Keywords: diabetes, health care expenditure, hypercholesterolemia, hypertension, medication adherence

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1. Introduction

Poor adherence to prescribed medication therapy and associated consequences is a long-standing problem.^[1] For over 50 years, health practitioners, payers, researchers, and policy makers have recognized the importance of taking therapies as prescribed. For example, 1 systematic review examined studies of interventions to improve patients' adherence dating from 1977,^[2] yet the problem persists.

One important reason to address poor medication adherence is that it is expensive. Health care spending in the United States (US) grew by 4.6% in 2018 to \$3.6 trillion, resulting in an average of \$11,172 per person. Prescription drugs represent a substantial portion of this figure, with the Centers for Medicare and Medicaid Services spending \$154.9 billion on Medicare Part D, \$30.4 billion in Medicare Part B, and \$67.6 billion in Medicaid for prescription drugs in 2017.^[3,4] Failure to take medications as prescribed is costly, with estimates ranging from \$100 to \$300 billion in direct costs, indirect costs, and opportunity costs, accounting for a substantial portion of avoidable health care costs.^[5–8] Furthermore, nonadherence rates as high as 50% have been reported.^[5,9] Thus, medication nonadherence remains an ongoing serious problem in health care today.

In addition, approximately 60% of US adults have at least 1 chronic condition and 40% have 2 or more chronic conditions.^[10] Chronic conditions are particularly problematic given that patients must take medications long term to realize associated health benefits, yet existing literature shows that adherence to long-term medication therapy for chronic diseases is often poor. For example, an observational study examining medication cost and total medical costs over 1 year in patients who had diabetes, heart failure, hypercholesterolemia, or hypertension reported mixed results based on levels of adherence. Individuals with hypercholesterolemia or diabetes who exhibited a high level of adherence had lower disease specific medical costs and total health care expenditures. For hypertension, high levels of adherence resulted in lower medical costs but no reduction in total costs; and there was no association between adherence and costs in individuals with heart failure.^[11]

Among Medicaid beneficiaries with hypertension, the association of adherence (using the medication possession ratio) and health care expenditures has also been assessed over a 36-month period.^[12] As with the study by Sokol et al,^[11] the association between high adherence and expenditures was mixed. Total health care costs were higher in individuals with high or low adherence, but lower in patients with moderate adherence.

A further study examined the association between medication adherence and multiple health services including inpatient hospitalizations, emergency department visits, and outpatient visits in patients who had at least 1 of 7 possible chronic conditions.^[13] Generally, greater adherence (using the continuous proportion of days covered (PDC) measure) was associated with fewer counts of health services utilization, except for dyslipidemia.

Although determining the association of adherence to medication therapy in patients who have chronic diseases is not new, 3 Pharmacy Quality Alliance (PQA) adherence measures for diabetes, hypertension, and cholesterol medications have been included in the Centers for Medicare and Medicaid Services Medicare Part D Star Ratings.^[14] The burden of nonadherence is increasingly important to stakeholders, as reimbursement may be tied to adherence performance measures. However, the definitions used in PQA medication adherence measures to outcomes has not been previously tested.

The purpose of this project was to assess the relationship between adherence definitions used in the following PQA adherence measures: PDC Renin Angiotensin System (RAS) Antagonists, PDC Statins, and PDC Diabetes All Class, and health care utilization and expenditures in a Medicare population with supplemental (optional private insurance plan that helps pay for costs that Medicare doesn't cover) and Part D (prescription drug insurance) coverage over a 1-year timeframe.

2. Methods

2.1. Study design & data source

This retrospective cohort study used a subset of IBM MarketScan Medicare Supplemental Research Databases (2009–2015) to assess the relationship between adherences, calculated using the standardized PQA adherence measure methodology, and health care utilization and expenditures. This dataset contained de-identified health care data for over 250 million US individuals.^[15] A customized dataset was obtained for this study that included individuals covered by Medicare Supplemental insurance plans in the United States who had prescription claim(s) for any: RAS antagonist, statin, or noninsulin diabetes medications between January 1, 2009 and December 31, 2015. De-identified data elements included: demographics, enrollment details, medical diagnoses and procedures; and prescription, inpatient, and outpatient administrative claims.^[16] The University of Arizona Institutional Review Board approved this study.

2.2. Study sample

Three cohorts were constructed according to the PQA adherence measure specifications, and included individuals who received a: RAS antagonist, statin, or diabetes medication; an individual in the dataset could be classified into more than 1 cohort. For each therapeutic class, the index date was defined as the first fill for a medication included in the PQA adherence measure after a 180-day baseline period. Individuals 18 years of age or older at the index date were eligible for inclusion. Individuals were included in the cohort if they had: continuous enrollment for 6 months prior to and 12 months after the index date, and at least 2 prescriptions dispensed for any medication included in the PQA measure, with at least 150 days between the first and last fill during the measurement period. Individuals were excluded from the cohort if they had a diagnosis of end-stage renal disease based on the international classification of diseases – ninth edition clinical modification code of 585.6 during the measurement period. For the diabetes cohort, individuals utilizing insulin products (identified through pharmacy claims data) during the measurement period were excluded. Individuals meeting all inclusion criteria were followed over a 1-year, postindex measurement period.

2.3. Outcome variables

Researchers investigated the effect of adherence on health care utilization and expenditures. Health care utilization was calculated as the number of outpatient and inpatient visits during the measurement period. All-cause health care expenditures were calculated for outpatient, inpatient, prescription drug, and total health care costs over the measurement period and were adjusted to 2015 US dollars.^[17]

2.4. Independent variable

The key independent variable was adherence status (adherent versus nonadherent). Adherence was measured using the standardized methodology described in the PDC Diabetes All Class (ie, biguanides, sulfonylureas, meglitinides, D-phenylalanine derivatives, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, alpha-glucosidase inhibitors), PDC Statins, and PDC Renin Angiotensin System Antagonists medication adherence measures (See Table , Supplemental Digital Content, <http://links.lww.com/MD2/A372> which lists the drugs included in the PQA adherence measures).^[18,19] PDC is the proportion of days in the study period that the treatment regimen is available to the individual as observed from pharmacy claims data. Individuals were considered adherent if the PDC was greater than or equal to 80% during the measurement period, in alignment with the PQA adherence measure specifications.

2.5. Adjusting variables

Potential confounders and risk factors for health care utilization and expenditures were included as adjusting variables in statistical models. Variables measured during the baseline period included: age (in years at index date); sex; geographic region; insurance type; Deyo-Charlson Comorbidity Index; the monthly average number of chronic medications; and treatment naïve status. Individuals were categorized as “treatment naïve” if they did not fill a prescription for a medication included in the respective PQA adherence measure during the baseline period. The monthly average number of chronic medications (with a prescription days’ supply greater than or equal to 28) was calculated to represent medication burden. In the statin cohort, type, and dose were used to classify statin treatment intensity into 3 groups (low, intermediate, and high) based on clinical guidelines.^[20] In the diabetes cohort, the average number of noninsulin medications used during the study period was calculated to account for differences in treatment intensity.

2.6. Statistical analysis

Generalized linear models (GLM) were used to test the relationship between the key independent variable (adherence status) and adjusting variables on continuous outcomes. A GLM with a log link and negative binomial distribution was used to assess the relationship between adherence status and health care resource utilization. A GLM with log link and gamma distribution assessed the relationship between adherence status and health care expenditures. Beta coefficients from GLMs were used to compute rate ratios (RR) and cost ratios (CR) to examine the difference in health care utilization and expenditure between the adherent and nonadherent groups.^[21] Fully adjusted model results are reported. Subject characteristics were assessed using *t* tests or Wilcoxon rank sum tests for continuous variables, and chi-square tests for categorical variables. An alpha level of 0.001 was set a priori for all analyses due to the large sample size and number of adjusting variables. All analyses were conducted using SASTM Version 9.4.z (SAS Institute, Cary, NC).

3. Results

3.1. Subject characteristic

Of the 4.5 million individuals with prescription claims data in the Medicare Supplemental MarketScan databases between 2009

and 2015, a total of 1,854,025 were included in the RAS antagonist cohort, 1,914,305 in the statin cohort, and 567,391 in the diabetes cohort. Figure 1 outlines the cohort inclusion criteria.

Table 1 describes the subject characteristics of the 3 cohorts by adherence status with adherent subjects constituting higher percentages of the RAS antagonist (n=1,479,308, 79.8%), statin (n=1,433,959, 74.9%), and diabetes (n=455,537, 80.3%) cohorts. The average age of subjects was similar between adherent and nonadherent groups (eg, 73.6 years and 73.8 years for RAS antagonist users). Gender distribution was well balanced in the adherent and nonadherent subjects (eg, males: 47.1% and 46.0% for RAS antagonist users).

The adherent and nonadherent groups were mostly from the North Central (eg, 30.3% and 31.7% in RAS antagonist users) and South (eg, 30.3% and 31.8% in RAS antagonist users) regions of the US. Both groups were mainly insured by preferred provider organizations (eg, 42.8% and 43.4% in RAS antagonist users) and comprehensive (eg, 37.1% and 36.1% in RAS antagonist users) health plans. Low Charlson Comorbidity Index scores (≤ 1) were prevalent in both groups.

The median number of chronic medications among adherent subjects at baseline was consistently higher than nonadherent subjects across all disease states (4.5 vs 3.5 for RAS antagonist users; 4.5 vs 3.5 for statin users; and 5.5 vs 4.0 for diabetes medication users). Nonadherent subjects had a higher proportion of those classified as treatment naïve (never received treatment for specific condition) than adherent subjects across the 3 cohorts (38.3% vs 21.8% for RAS antagonist users, 39.6% vs 20.8% for statin users; and 47.6% vs 24.1% for diabetes medication users).

There were statistically significant differences between the adherent and nonadherent groups for all characteristics in all 3 cohorts ($P < .001$) except for the mean age in the diabetes cohort ($P = .1166$).

3.2. Descriptive analyses

During the study period, adherent subjects had a lower number of outpatient (13.0 [standard deviation, SD=14.0] vs 15.0 [SD=16.7]; 17.9 [SD=16.2] vs 19.0 [SD=18.0]; and 18.6 [SD=16.1] vs 19.5 [SD=18.0]) and inpatient (0.2 [SD=0.7] vs 0.4 [SD=1.0]; 0.2 [SD=0.7] vs 0.3 [SD=0.9]; and 0.2 [SD=0.7] vs 0.3 [SD=0.9]) visits than nonadherent subjects for the RAS antagonist, statin, and diabetes cohorts, respectively. Regardless of disease state, adherent subjects experienced lower mean total expenditure than nonadherent subjects (\$13,231 [SD=27,658] vs. \$16,976 [SD=36,732] for RAS antagonist users; \$13,722 [SD=26,672] vs. \$15,631 [SD=35,303] for statin users; and \$14,094 [SD=28,319] vs. \$15,424 [SD=34,864] for diabetes medication users). For each type of expenditure, descriptive statistics showed that adherent subjects had lower outpatient and inpatient expenditures yet had higher prescription drug costs than nonadherent subjects. Such findings were consistent across 3 disease states. All differences between adherent and nonadherent groups were significant at $P < .001$ (Table 1).

3.3. Effect of adherence on health care utilization and expenditure

Table 2 presents the effect of adherence on health care utilization and expenditure. Generally, the magnitude of adherence effects differed by disease state with the most pronounced effect observed in the RAS antagonist cohort.

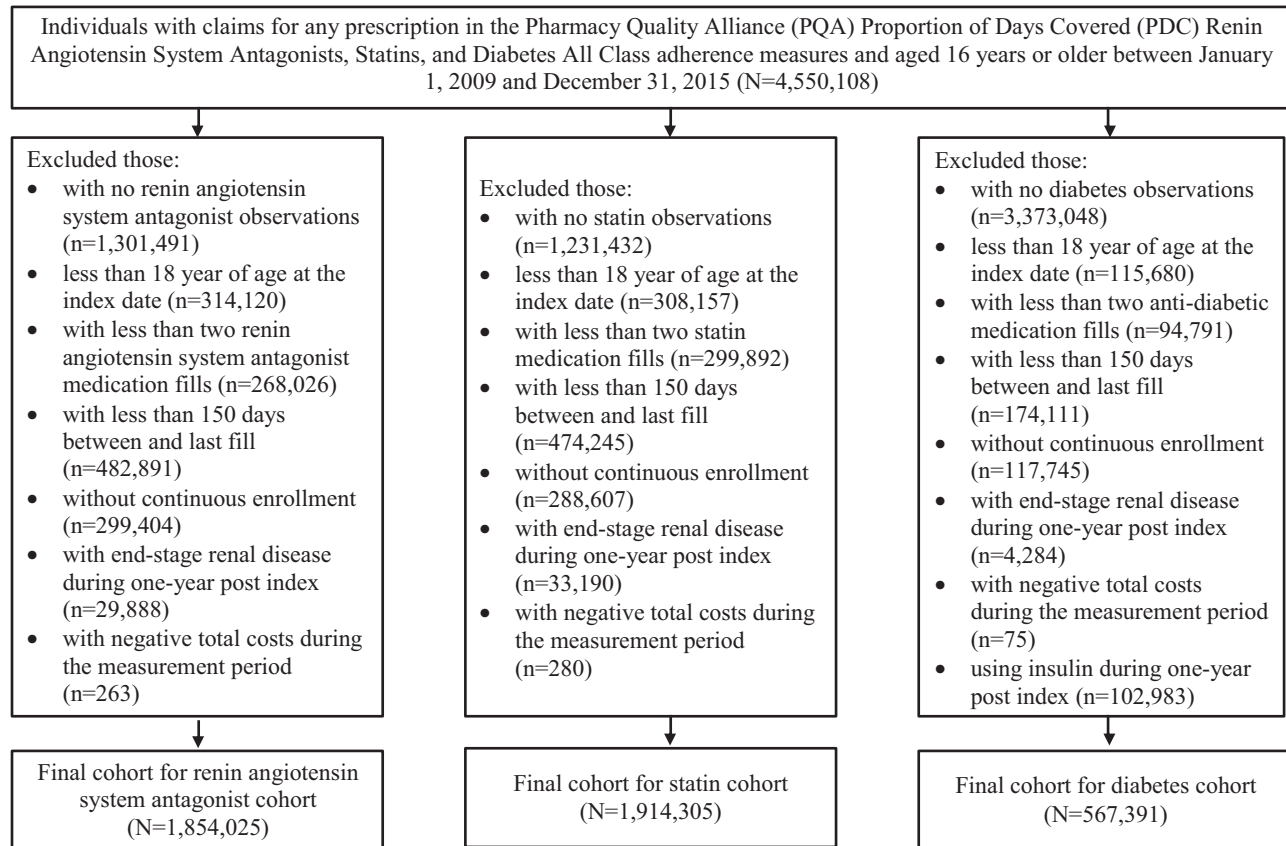


Figure 1. Cohort flowchart diagram (2009–2015).

Across the 3 disease states, adherence (PDC \geq 80%) was associated with significantly lower outpatient service use compared to nonadherence, ranging from 3.0% (RR = 0.970, 95% confidence interval [CI] = 0.964, 0.975) fewer visits for the diabetes medication cohort to 12.1% (RR = 0.879, 95% CI = 0.875, 0.882) fewer visits for the RAS antagonist cohort. Additionally, inpatient visits were proportionally lower among adherent individuals (41.5% for RAS antagonist, 30.3% for statin, and 18.9% for diabetes medication cohorts).

Adherence was significantly associated with health care expenditures. In all 3 disease states, adherence was associated with lower: outpatient expenditure by 20.3% (CR = 0.797, 95% CI = 0.794, 0.800) in the RAS antagonist cohort, 14.5% (CR = 0.855, 95% CI = 0.853, 0.858) in the statin cohort, and 9% (CR = 0.904, 95% CI = 0.898, 0.911) in the diabetes medication cohort; and inpatient expenditure by 41.9% (CR = 0.581, 95% CI = 0.579, 0.583) in the RAS antagonist cohort, 29.8% (CR = 0.702, 95% CI = 0.700, 0.705) in the statin cohort, and 20.0% (CR = 0.795, 95% CI = 0.789, 0.801) in the diabetes medication cohort, compared to those classified as nonadherent.

Unlike outpatient and inpatient expenditures, the adherent group was associated with higher prescription drug expenditure by 9.8% (CR = 1.098, 95% CI = 1.094, 1.102) for the RAS antagonist cohort, 12.2% (CR = 1.122, 95% CI = 1.118, 1.126) for the statin cohort, and 6.7% (CR = 1.067, 95% CI = 1.059, 1.075) for the diabetes medication cohort, compared to the nonadherent group.

In all disease states, the total expenditure was significantly lower for adherent subjects. The adherent RAS antagonist subjects had the most reduction (22.9%) (CR = 0.771, 95% CI = 0.768, 0.773) in total expenditures, followed by 14.5% reduction for statin users (CR = 0.855, 95% CI = 0.852, 0.858) and 11% reduction for diabetes medication users (CR = 0.882, 95% CI = 0.875, 0.888).

3.4. Incremental cost per member per month

To give monetary context to the effect of adherence, the average incremental cost per member per month (PMPM) was computed based on the CR and annual average spending from each type of expenditure (ie, outpatient, inpatient, drug, total expenditure). The average incremental cost PMPM for adherent subjects is depicted in Figure 2.

Except for prescription drug expenditure, the cost saving associated with adherence was most notable in the RAS antagonist and least in the diabetes cohort. For outpatient expenditure, monthly per member savings were highest (incremental cost PMPM = \$136.40) in RAS antagonist users and lowest (incremental cost PMPM = \$60.18) in diabetes medication users. The incremental PMPM of inpatient expenditure ranged from \$211.92 (RAS antagonist users) to \$85.94 (diabetes medication users).

As anticipated, adherence was associated with higher drug expenditure PMPM by: \$23.34 for RAS antagonist, \$29.13 for

Table 1
Characteristics of adherent vs nonadherent Medicare beneficiaries.

Characteristic	Renin-angiotensin system antagonists		Statins		Diabetes medications	
	Adherent (n=1,479,308)	Nonadherent (n=374,717)	Adherent (n=1,433,959)	Nonadherent (n=480,346)	Adherent (n=455,537)	Nonadherent (n=111,854)
Age (in yr), mean (SD)	73.6 (7.5)	73.8 (7.8)	73.4 (7.3)	73.1 (7.3)	72.9 (7.0)*	72.9 (7.2)*
Male gender, N (%)	696,931 (47.1)	172,405 (46.0)	718,876 (50.1)	217,999 (45.4)	242,211 (53.2)	53,889 (48.2)
Region, N (%)						
Northeast	331,475 (22.4)	72,345 (19.3)	319,550 (22.3)	101,949 (21.2)	96,158 (21.1)	20,986 (18.8)
North Central	448,226 (30.3)	118,618 (31.7)	422,964 (29.5)	143,551 (29.9)	141,586 (31.1)	36,077 (32.3)
South	448,816 (30.3)	119,169 (31.8)	431,759 (30.1)	152,125 (31.7)	140,205 (30.8)	36,354 (32.5)
West	246,325 (16.7)	63,349 (16.9)	249,772 (17.4)	78,914 (16.4)	73,476 (16.1)	17,350 (15.5)
Unknown	4466 (0.3)	1236 (0.3)	9914 (0.7)	3807 (0.8)	4112 (0.9)	1087 (1.0)
Plan type, N (%)						
Comprehensive	548,892 (37.1)	135,429 (36.1)	532,438 (37.1)	167,221 (34.8)	143,494 (31.5)	33,154 (29.6)
Health maintenance organization	210,977 (14.3)	55,483 (14.8)	202,443 (14.1)	73,215 (15.2)	68,304 (15.0)	17,872 (16.0)
Point of service	47,250 (3.2)	11,542 (3.1)	45,447 (3.2)	14,705 (3.1)	14,556 (3.2)	3539 (3.2)
Preferred provider organization	632,829 (42.8)	162,545 (43.4)	614,702 (42.9)	213,119 (44.4)	216,253 (47.5)	54,423 (48.7)
Other	16,952 (1.2)	4539 (1.3)	16,562 (1.2)	5679 (1.2)	4750 (1.0)	1184 (1.1)
Unknown	22,408 (1.5)	5179 (1.4)	22,367 (1.6)	6407 (1.3)	8180 (1.8)	1682 (1.5)
Deyo-Charlson Comorbidity Index Score, N (%)						
0	729,664 (49.3)	175,777 (46.9)	710,626 (49.6)	234,497 (48.8)	80,328 (17.6)	23,060 (20.6)
1	380,240 (25.7)	96,769 (25.8)	359,386 (25.1)	122,207 (25.4)	208,133 (45.7)	48,094 (43.0)
2	182,796 (12.4)	47,893 (12.8)	179,146 (12.5)	59,558 (12.4)	61,829 (13.6)	16,392 (14.7)
3	108,636 (7.3)	29,644 (7.9)	105,272 (7.3)	35,679 (7.4)	62,941 (13.8)	13,779 (12.3)
4	37,898 (2.6)	11,489 (3.1)	38,332 (2.7)	13,426 (2.8)	20,720 (4.5)	5,115 (4.6)
5+	40,074 (2.7)	13,145 (3.5)	41,197 (2.9)	14,979 (3.1)	21,586 (4.7)	5,414 (4.8)
Treatment naive, N (%)	322,146 (21.8)	143,536 (38.3)	298,514 (20.8)	190,394 (39.6)	109,869 (24.1)	53,213 (47.6)
Average number of chronic medications in baseline, median (interquartile range)	4.5 (3.8)	3.5 (3.7)	4.5 (3.7)	3.5 (3.7)	5.5 (4.0)	4.0 (3.8)
Intensity	-	-	1,060,680 (74.0)	349,525 (72.8)	1.3 (0.8)	0.8 (0.3)
Utilization in study period mean (SD)^a						
Outpatient	13.0 (14.0)	15.0 (16.7)	17.9 (16.2)	19.0 (18.0)	18.6 (16.1)	19.5 (18.0)
Inpatient	0.2 (0.7)	0.4 (1.0)	0.2 (0.7)	0.3 (0.9)	0.2 (0.7)	0.3 (0.9)
Expenditure in study period mean (SD)^b						
Outpatient	6309 (17,431)	8063 (18,616)	6448 (14,790)	7465 (17,222)	6462 (18,433)	7546 (19,900)
Inpatient	3503 (16,931)	6066 (25,691)	3687 (17,526)	5298 (25,302)	3555 (16,715)	5026 (22,916)
Drug	3420 (5,583)	2847 (5,746)	3586 (5,491)	2867 (5,227)	4077 (5,766)	2852 (5,832)
Total	13,231 (27,658)	16,976 (36,732)	13,722 (26,672)	15,631 (35,303)	14,094 (28,319)	15,424 (34,864)

All differences in characteristic, utilization, and expenditure were significant at the $P < .001$ level unless otherwise noted. * $P = .1166$.

Other health plans incorporates those that were reported by less than 1% of subjects, which includes: exclusive provider organization; point of service with capitation; consumer-directed health plan; high deductible health plan.

Intensity refers to the number of moderate intensity statin medications in study period, N (%), and the average number of diabetic medications in study period, median (interquartile range). There is no intensity measure for hypertension.

SD = standard deviation, - = not applicable.

^a Outpatient utilization includes laboratory tests, office visits, and other outpatient services; inpatient utilization includes inpatient admissions, emergency department use, and other inpatient services.

^b 2015 United States Dollars.

statin, and \$16.00 for diabetes medication cohorts. Overall, adherence was associated with a \$324.53, \$188.62, and \$152.19 savings in RAS antagonist, statin, and diabetes medication cohorts, respectively.

4. Discussion

This study adds to the evidence base regarding the effect of adherence, using standardized methodologies and definitions used in PQA quality measures, on health care utilization and expenditure over a 1-year period among US Medicare supplemental populations. The shift to value-driven, quality-based health care by policymakers has incentivized providers to improve adherence, in a large part, to decrease wasted health care dollars. Chronic conditions including cardiovascular disease, hypertension, and diabetes are major contributors to

these costs, and there is substantial research showing the impact of programs that improve adherence for these disease states.^[8,22]

This project addressed a gap in the literature by investigating the association between adherence (assessed via PQA PDC medication adherence measures) and economic outcomes over a 1-year timeframe.

While much research has investigated the reasons for nonadherence to medication regimens,^[22-26] little exists on evaluating the impact of adherence on health care utilization and costs over a short-term (eg, 1-year) period. Gibson et al^[27] investigated the impact of a value-based insurance design program with decreased prescription cost sharing and found improved adherence to medications yet they did not examine utilization. A systematic review of the impact of lowering medication copayments found that adherence improved, yet a limited number of studies examined economic outcomes^[26] and

Table 2
Healthcare utilization and expenditure generalized linear model results.

Utilization ^a	Renin-angiotensin system antagonists		Statins		Diabetes medications	
	Risk ratio (95% CI)	%Δ	Risk ratio (95% CI)	%Δ	Risk ratio (95% CI)	%Δ
Outpatient	0.879 (0.875, 0.882)	-12.1	0.931 (0.929, 0.934)	-6.9	0.970 (0.964, 0.975)	-3.0
Inpatient	0.585 (0.580, 0.591)	-41.5	0.697 (0.690, 0.703)	-30.3	0.811 (0.794, 0.828)	-18.9
Expenditure ^b	Cost ratio (95% CI)	%Δ	Cost ratio (95% CI)	%Δ	Cost ratio (95% CI)	%Δ
Outpatient	0.797 (0.794, 0.800)	-20.3	0.855 (0.853, 0.858)	-14.5	0.904 (0.898, 0.911)	-9.0
Inpatient	0.581 (0.579, 0.583)	-41.9	0.702 (0.700, 0.705)	-29.8	0.795 (0.789, 0.801)	-20.0
Drug	1.098 (1.094, 1.102)	9.8	1.122 (1.118, 1.126)	12.2	1.067 (1.059, 1.075)	6.7
Total	0.771 (0.768, 0.773)	-22.9	0.855 (0.852, 0.858)	-14.5	0.882 (0.875, 0.888)	-11.0

CI = confidence interval, %Δ = adherent group percent difference compared to nonadherent.

^a Generalized linear model with log link and negative binomial distribution adjusted for age, sex, plan type, region, Charlson comorbidity index, medication use status, average number of chronic medications at baseline per month, average number of PQA-measure medications during study period per month.

^b Generalized linear model with log link and gamma distribution adjusted for age, sex, plan type, region, Charlson comorbidity index, medication use status, average number of chronic medications at baseline per month, average number of PQA-measure medications during study period per month.

there was insufficient evidence to conclude a beneficial effect. Furthermore, systematic reviews studying the impact of adherence on economic outcomes are challenging due to design, disease state, and cost definition differences.^[8]

Studies assessing the impact of adherence on cost had important similarities and differences from the current study. Mojtabai and Olsson^[28] examined the relationship between the cost of medications, adherence, and outcomes in a Medicare population. Adherent versus nonadherent groups were defined depending on whether medication costs caused them to take less than directed. Outcomes were assessed across the same disease states as the current study. For each of the disease states, nonadherent Medicare beneficiaries perceived their overall health was worse, and were more likely to have been hospitalized than the adherent group. Patient perceptions are extremely important in medication-taking behavior, however, using an objective measure such as PDC in tandem with claims data allows for direct assessment of impact. Nevertheless, the current study findings parallel those of Mojtabai et al regarding greater utilization and expenditures among nonadherent individuals.

Fukada and Mizobe^[29] conducted a retrospective study of individuals with diabetes and used international classification of diseases methodology similar to the current study, however they broadly defined nonadherence as any period of no medication for up to 6 months rather than using PDC. Interestingly, they found no difference in expenditures between the adherent and nonadherent groups in the first year; however, in years 2 through 5, the adherent group had significantly less expenditures than the nonadherent group.

By leveraging the PQA PDC medication adherence measure specifications, the current study was able to detect differences between adherent and nonadherent individuals as early as the first year, with consistency in utilization and cost across the 3 medication classes (RAS antagonists, statins, and diabetes). For each of the 3 classes of drugs, adherence was associated with lower outpatient and inpatient utilization and costs, as well as lower total health care costs. Conversely, yet not surprisingly, adherence to each drug class was associated with higher prescription drug costs. This is a logical finding given that adherent individuals are taking their medication, and thus

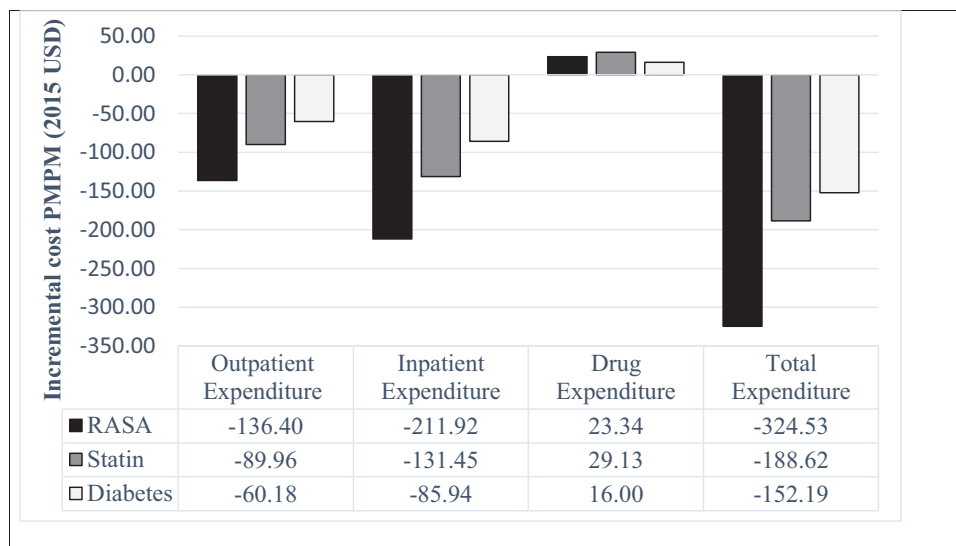


Figure 2. Adherence incremental cost per member per month. RASA=Renin-angiotensin system antagonist.

incurring higher prescription drug costs than those not taking their medications (ie, nonadherent individuals). In the context of overall costs however, it appears that the higher expenditure associated with taking prescription medications is warranted, given that medication adherence was associated with lower total health care expenditures.

The magnitude of variation in the effect of adherence across conditions was notable. The diabetes medication adherence measure was consistently associated with the smallest effect size, while the hypertension (RAS antagonist) measure had the largest. Adherence was associated with a reduction in outpatient service utilization, although this was lower than the associated reduction for inpatient utilization. Across measures, the effect of adherence on inpatient expenditures was the largest compared to other cost categories. Thus, these results provide evidence that adherence effects are possible within a brief timeframe, at least for these disease states. However, more work is needed to study these performance metrics (eg, RAS antagonists, statins, diabetes medications) in more diverse populations.

There were limitations to this study. This was a retrospective study of administrative claims data, and as such, was not designed to investigate adherence-related questions. Factors that may impact adherence (eg, patient socioeconomic status) and other relevant data (eg, laboratory test results) were not available in the dataset. Additionally, medication exposure based on filled prescriptions is an indirect measure of actual patient behavior and may not indicate that individuals consumed the obtained medications. Inclusion of total health care expenditures may have overestimated costs if claims data captured expenditures not directly related to the disease states. The data may have contained costs that were later reversed, and coding errors, and that could not be accounted for. While statistically significant, differences between groups were small, thus the effects could be potentially attributed to the large sample sizes.

Despite the limitations, the researchers feel that these claims data are a robust source of information. While this study focused on outcomes based on adherence to RAS antagonists, statins, and diabetes medications separately, if adherence was measured at the patient level with concurrent chronic diseases, it is feasible to assume the impact on outcomes may be greater. Motivating and ensuring adherence remains a challenge across the entire health care system. Further research as to the underlying reasons, or patient motivations, for nonadherence is required.^[30–33]

5. Conclusion

This study is one of the first to assess the impact of adherence, as specified by the PQA PDC Diabetes All Class, PDC Statins, and PDC Renin Angiotensin System Antagonists medication adherence measures in a Medicare supplemental population over a 1-year period. Several key findings were discovered: adherence has a large association on the likelihood of utilizing health care services and subsequent health care expenditure; and adherence varies by disease states. Additionally, this analysis quantified the economic effect of nonadherence to medication regimens in this population. Nonadherent populations with chronic diseases are associated with significantly more health care utilization and expenditures. These findings highlight the need for more effective adherence programs to achieve better outcomes for individuals while decreasing health care costs.

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References

- [1] Brown MT, Bussell JK. Medication adherence: WHO cares? *Mayo Clin Proc* 2011;86:304–14.
- [2] Roter DL, Hall JA, Merisca R, Nordstrom B, Cretin D, Svarstad B. Effectiveness of interventions to improve patient compliance: a meta-analysis. *Med Care* 1998;36:1138–61.
- [3] Centers for Medicare & Medicaid Services. National Health Expenditure Data, Historical. [CMS web site]. December 17, 2019. Available at: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical> Accessed November 6, 2020.
- [4] Centers for Medicare & Medicaid Services. CMS Drug Spending. [CMS web site]. December 19, 2019. Available at: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/index> Accessed November 6, 2020.
- [5] DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care* 2004;42:200–9.
- [6] Benjamin RM. Medication adherence: helping patients take their medicines as directed. *Public Health Rep* 2012;127:2–3.
- [7] Aitken M, Valkova S. Avoidable costs in US healthcare: the \$200 billion opportunity from using medicines more responsibly. [IMS Institute for Healthcare Informatics web site]. June 2013. Available at: http://offers.premierinc.com/rs/381-NBB-525/images/Avoidable_Costs_in%20_US_Healthcare-IHII_AvoidableCosts_2013%5B1%5D.pdf Accessed November 6, 2020.
- [8] Iuga AO, McGuire MJ. Adherence and health care costs. *Risk Manag Healthc Policy* 2014;7:35–44.
- [9] Haynes RB, McDonald HP, Garg A, Montague P. Interventions for helping patients to follow prescriptions for medications. *Cochrane Database Syst Rev* 2002;CD000011doi: 10.1002/14651858.CD000011.

- [10] Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP). About Chronic Diseases. [CDC web site]. October 7, 2020. Available at: <https://www.cdc.gov/chronicdisease/about/index.htm> Accessed November 6, 2020.
- [11] Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care* 2005;43:521–30.
- [12] Yang Z, Howard DH, Will J, Loustalot F, Ritchey F M, Roy F K. Association of antihypertensive medication adherence with healthcare use and Medicaid expenditures for acute cardiovascular events. *Med Care* 2016;54:504–11.
- [13] Roebuck MC, Kaestner RJ, Dougherty JS. Impact of medication adherence on health services utilization in Medicaid. *Med Care* 2018;56:266–73.
- [14] Pharmacy Quality Alliance. PQA has developed three new pharmacy performance measures, comments sought. [PQA web site]. December 18, 2019. Available at: <https://www.pqaalliance.org/new-pharmacy-performance-measures> Accessed November 6, 2020.
- [15] IBM. IBM MarketScan Research Databases. [IBM web site]. Available at: <https://www.ibm.com/us-en/marketplace/marketscan-research-databases> Accessed November 6, 2020.
- [16] IBM Watson Health. [IBM Watson Health web site]. April 2019. IBM MarketScan Research Databases for Health Services Researchers. Available at: <https://www.ibm.com/downloads/cas/6KNYVVQ2> Accessed August 10, 2021.
- [17] United States Department of Labor. Consumer Price Index (CPI) Databases. [U.S. Bureau of Labor Statistics web site]. Available at: <https://www.bls.gov/cpi/data.htm> Accessed November 6, 2020.
- [18] Nau DP. Proportion of days covered (PDC) as a preferred method of measuring medication adherence. Available at: https://www.researchgate.net/publication/273505401_Cost-effectiveness_Analysis_of_LDL_cholesterol-Lowering_Therapy_in_Hypertensive_Patients_with_Type-2_Diabetes_in_Korea_Single-Pill_Regimen_AmlodipineAtorvastatin_versus_Double-Pill_Regimen_Amlodipine_/fulltext/55d8d67908aed6a199a88e96/Cost-effectiveness-Analysis-of-LDLcholesterol-Lowering-Therapy-in-Hypertensive-Patients-with-Type-2-Diabetes-in-Korea-Single-Pill-Regimen-Amlodipine-Atorvastatin-versus-Double-Pill-Regimen-Amlodipine.pdf Accessed November 6, 2020.
- [19] Centers for Medicare and Medicaid Services. Part C and D Performance Data. [CMS web site]. October 22, 2020. Available at: <https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovgenin/performance.html> Accessed November 6, 2020.
- [20] Stone NJ, Robinson JG, Lichtenstein AH, et al. Treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: synopsis of the 2013 American College of Cardiology/American Heart Association cholesterol guideline. *Ann Intern Med* 2014;160:339–43.
- [21] Halvorsen R, Palmquist R. The interpretation of dummy variables in semilogarithmic equations. *Am Econ Rev* 1980;70:474–5.
- [22] Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence. *Am J Health Syst Pharm* 2003;60:657–65.
- [23] Bates TR, Connaughton VM, Watts GF. Non-adherence to statin therapy: a major challenge for preventive cardiology. *Expert Opin Pharmacother* 2009;10:2973–85.
- [24] Conn VS, Hafdahl AR, Cooper PS, Ruppert TM, Mehr DR, Russell CL. Interventions to improve medication adherence among older adults: meta-analysis of adherence outcomes among randomized controlled trials. *Gerontologist* 2009;49:447–62.
- [25] DeFulio A, Silverman K. The use of incentives to reinforce medication adherence. *Prev Med* 2012;55:S86–94.
- [26] Mann BS, Barnieh L, Tang K, et al. Association between drug insurance cost sharing strategies and outcomes in patients with chronic diseases: a systematic review. *PLoS One* 2014;9:e89168.
- [27] Gibson TB, Wang S, Kelly E, et al. A value-based insurance design program at a large company boosted medication adherence for employees with chronic illnesses. *Health Aff* 2011;30:109–17.
- [28] Mojtabai R, Olfson M. Medication costs, adherence, and health outcomes among Medicare beneficiaries. *Health Aff* 2003;22:220–9.
- [29] Fukuda H, Mizobe M. Impact of nonadherence on complication risks and healthcare costs in patients newly-diagnosed with diabetes. *Diabetes Res Clin Pract* 2017;123:55–62.
- [30] Cutler DM, Everett W. Thinking outside the pillbox—medication adherence as a priority for health care reform. *N Engl J Med* 2010;362:1553–5.
- [31] Nieuwlaat R, Wilczynski N, Navarro T, et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2014; CD000011.
- [32] National Community Pharmacists Association. Medication Adherence in America: A National Report. [National Community Pharmacists Association web site]. 2013. Available at: http://www.ncpa.co/adherence/AdherenceReportCard_Abridged.pdf Accessed November 6, 2020.
- [33] Kleinsinger F. The unmet challenge of medication nonadherence. *Perm J* 2018;22:18–33.