

Effect of Antihypertensive Medication Adherence Among Employees With Hypertension

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Hypertension affected 73.6 million US adults in 2006,¹ up from 65 million 6 years earlier.² One in 3 US adults has hypertension.³ High blood pressure is a precursor to many serious health conditions such as coronary heart disease,⁴ heart failure,⁵ and stroke,⁶ and has an overall death rate of 17.9%.¹ Besides its health influences, hypertension has financial effects.⁷ The direct and indirect costs of hypertension for 2008 were expected to total \$69.4 billion, making hypertension the second most costly cardiovascular-related disorder.^{1,8}

There is strong evidence that prescription drugs provide clinical value for treatment of hypertension.^{9,10} For example, pharmacologic treatment of hypertension reduces the risk of stroke, coronary events, heart failure, and progression of renal disease.^{9,11-17} On the other hand, there is evidence that hypertension is a major driver of drug spending in many countries.¹⁸ Employers want to know whether antihypertensive medications are cost-effective, if drug treatment reduces overall healthcare costs, and whether hypertension medication adherence reduces patients' need for expensive cardiovascular services, hospitalizations, and emergency department treatment.

Results have shown that antihypertensive drug therapy is an important factor in containing the costs of managing hypertension and its complications.¹⁷ However, the therapeutic and economic benefits of drug treatment are often demonstrated in the controlled settings of clinical trials. These benefits may not be realized in day-to-day practice, wherein the cost-effectiveness of drug therapy may fail because of factors such as inadequate blood pressure control,^{14,17} discontinuation of or switching between therapies,¹⁹ and poor compliance.^{10,20}

Nonadherence to antihypertensive drugs is high,²¹⁻²⁶ with possibly substantial economic consequences.²⁶ When conditions are treated suboptimally, symptoms and complications may worsen, leading to increased use of hospital and emergency department services, office visits, and other medical resources.^{24,27} For some chronic conditions, including hypertension, there is evidence that increased adherence may generate medical savings that more than offset the associated increases in drug costs.^{22,28-31}

Few studies have measured the cost-effectiveness of medication adherence for treatment provided under benefit plans in employed population settings, although some studies^{21,32-36}

Objectives: To determine if antihypertensive medication adherence is associated with decreased medical and drug costs, medical service utilization, and work absence days.

Study Design: Retrospective database study using medical, pharmacy, sick leave, short-term and long-term disability, and workers' compensation claims data from multiple large US employers from 2001 to 2008.

Methods: We used medical and pharmacy claims to identify employees with hypertension. The index date was the date of the first hypertension-related pharmacy claim. Eligible employees had health plan enrollment 6 months before the index date and at least 12 months after the index date. Employees younger than 45 years were excluded from the study. Regression models estimated the effect of the proportion of days covered (PDC) by hypertension medication on outcomes after the index date, including health benefit costs, medical service utilization, and work absence days, as well as some clinical outcomes calculated separately for high-prior-cost and low-prior-cost employees. High-prior-cost employees were those who accounted for the top 60.0% of total medical costs during the 6 months before the index date. The regression models controlled for demographics, job-related variables, and comorbidities.

Results: Among low-prior-cost employees, high PDC was associated with increased medical and drug costs and work absence days. Among high-prior-cost employees, high PDC was associated with decreased medical and drug costs, fewer work absence days and inpatient hospital days, and increased hypertension-specific medical costs.

Conclusion: Antihypertensive medication adherence was associated with improvement in some short-term utilization measures among high-prior-cost employees, but significant short-term improvement was not seen among low-prior-cost employees.

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Take-Away Points

Increased antihypertensive medication adherence was associated with several improved short-term outcomes among the 4.6% of employees with the highest prior medical costs.

- The improvements included lower total medical and drug costs, fewer medical services, and decreased inpatient hospital days.
- Because these improved short-term outcomes were not seen among employees with low prior medical costs, specialized care management by subpopulation may be required.

have attempted to measure the effect on healthcare costs of drug use reduction following imposition of coverage limits or copayment requirements in Medicaid settings. To our knowledge, a single study¹⁸ has evaluated the relationships among antihypertensive medication adherence, medical services utilization, and healthcare costs among a large benefit plan population. The results showed that all-cause medical costs and hospitalization rates were significantly lower for patients with high medication adherence.¹⁸

The primary objective of this study was to quantify the relationship between antihypertensive medication adherence and health benefit costs, medical service utilization, work absence days, and certain clinical outcomes such as stroke, myocardial infarction, and cardiovascular procedures. This study adds to the compliance literature by measuring a broader set of outcomes relevant to employers than previously studied, including medical and drug costs and utilization, work absence days because of sick leave, short-term and long-term disability, and workers' compensation claims, as well as clinical outcomes for high-prior-cost and low-prior-cost employees.

METHODS

Research Population and Cohort Definitions

The patients included in the study are derived from more than 670,000 employees across the United States whose health benefits, salary, and demographic data are maintained in the Human Capital Management Services Research Reference Database at an employee level. The data used in this study are from 2001 to 2008.

The study cohort (employees with hypertension) was defined using health insurance claims data for healthcare services and prescription drug claims. Employees with hypertension were identified using any of the following inclusion criteria: (1) at least 2 medical claims (any kind) for hypertension (primary, secondary, or tertiary *International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code of 401.xx), (2) an emergency department visit with a primary diagnosis of hypertension, or (3) an inpatient admission with a primary diagnosis of hypertension. In addition, all employees were required to have

a hypertension maintenance medication prescription (antihypertensive, diuretic, β -blocker, angiotensin-converting enzyme inhibitor, calcium channel blocker, or α -agonist or α -blocker). A flowchart summarizing the selection of employees based on the eligibility requirements is given in **Table 1**.

The date of the first hypertension prescription among the data was defined as the employee's index date. The first hypertension medical claim was required to occur any time before 1 year after the index date. The measurements of medical and drug costs, medical service utilization, and work absence days were generally made over a 12-month period beginning at the index date. The measurements of clinical outcomes (stroke, myocardial infarction, and cardiovascular procedures) were made over a 24-month period beginning at the index date. Employees in the study cohort were required to be at least 45 years of age on the index date and to be employed and enrolled in a health insurance plan from 6 months before to at least 12 months (≥ 24 months for clinical outcomes) after the index date.

Descriptive Statistics

Descriptive variables were examined to provide information on demographic characteristics and on certain health-care utilization and copayment values of the study cohort. In addition, data on subcohorts were included in the analysis of each particular outcome.

Hypertension-Related Drug Use

The study examined the number of employees using each class of hypertension-related medication. The proportion of days covered (PDC) was calculated directly from the days supply information in the claims data for all employees for the 12-month period after the index date as follows: the number of days each employee had a supply of any hypertension-related medication available divided by the number of days in the measurement year. Overlap periods (days when the employee possessed >1 type of hypertension-related medication) were not counted twice.

Effect of PDC on Outcomes

Regression techniques were used to estimate the effect of PDC during 12 or 24 months after the index date on the following 9 outcome (dependent) variables: (1) annual (year after the index date) medical and drug costs; (2) annual hypertension-specific (ICD-9-CM code 401.xx) medical costs; (3) the annual number of medical services; (4) the annual number of inpatient hospital days; (5) annual number of work absence days because of sick leave, short-term disability,

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Table 1. Employee Selection Flowchart

Selection Requirements	Sample Size
Employees in Human Capital Management Services Research Reference Database	677,813
Employees having ≥ 2 outpatient medical claims (primary, secondary, or tertiary ICD-9-CM code) for hypertension or an emergency department visit or inpatient admission with a primary diagnosis of hypertension	86,396
Employees (from the above sample) who also had a hypertension medication prescription	64,865
Employees (from the above sample) whose first hypertension medical claim occurred any time before 1 y after the index date	56,601
Employees (from the above sample) who were employed and enrolled in a health insurance plan from 6 mo before to ≥ 12 mo after the index date	11,880
Employees (from the above sample) who were aged ≥ 45 y on the index date	6494
Employees (from the above sample) who had proportion of days covered > 0	6244
Employees (from the above sample) who had no missing data for all control variables	6236

ICD-9-CM indicates International Classification of Diseases, Ninth Revision, Clinical Modification.

ity, long-term disability, or workers' compensation; (6) annual probability of a workers' compensation claim; (7) 2-year (after the index date) probability of a stroke; (8) 2-year probability of a myocardial infarction; and (9) 2-year probability of a cardiovascular procedure (coronary artery bypass, percutaneous transluminal coronary angioplasty, or coronary stents).

Medical costs included all insurance payments for all medical services as recorded in the health insurance claims data. Drug (pharmacy) costs included all insurance payments for all drug costs as recorded in the health insurance claims data. Hypertension-specific medical costs included all insurance payments for medical claims with a primary diagnosis of hypertension. All costs were inflation adjusted to 2008 US dollars. Measurement of annual work absence days because of sick leave, short-term disability, long-term disability, and workers' compensation was based on payroll records and on disability carriers' claims data.

Regression methods were used to measure the association between outcomes and PDC (measured as a continuous variable). Generalized linear models with a gamma distribution and log link were used to estimate the level of continuous (medical and drug costs, medical service utilization, and work absence days) outcomes. Logistic regression analysis was used to predict the likelihood of having any dichotomous outcome (workers' compensation claim, stroke, myocardial infarction, or cardiovascular procedure). Only employees eligible for a given benefit were included in the regression models used to estimate medical and drug costs or work absence days from that benefit type. In the models for stroke, myocardial infarction, and cardiovascular procedures, employees with these events in the 6 months before the index date and employees with fewer than 24 months of health plan enrollment after the index date were excluded.

The objective of these models was to determine if PDC is associated with any of the aforementioned outcomes, after con-

trolling for the following: age, sex, salary, location of residence, proportion of hypertension-related medication claims filled using mail order versus retail pharmacy, amount of employee copayments for hypertension-related medications, the number of other (nonhypertension) medications, month of the index date, emergency department use during 6 months before the index date, and the Charlson Comorbidity Index (and specific indicators for diabetes mellitus, hyperlipidemia, myocardial infarction, and chronic heart failure). Because medical costs before the index date were found to be strongly associated with most outcomes in the study, these analyses were performed separately for employees with high versus low total medical costs in the 6 months before the index date. The cutoff between high prior cost and low prior cost was determined by identifying the highest-cost employees (who accounted for the top 60.0% of total medical costs before the index date [top 3 "cost quintiles," or 4.6% of the population]), and separating them from the lowest-cost employees (who accounted for the remaining 40.0% of total medical costs before the index date). To obtain a solid model for each outcome and subgroup, the following approach was used. We initially included in the model all of the aforementioned control variables and then used the automatic "stepwise" variable selection function to maintain in the model only those variables that had significant association with the outcome. As a result, the specific models for different outcomes and subgroups have different sets of control variables.

RESULTS

Descriptive Statistics

The study cohort included 6236 employees, all of whom had health plan enrollment from 6 months before their index date to at least 12 months after. The flowchart in Table

■ **Table 2.** Descriptive Statistics for Employees in the Study Cohort and Subcohorts

Variable	Study Cohort (N = 6236)	Subcohort			
		Annual No. of Inpatient Hospital Days (n = 4942)	Annual No. of Work Absence Days (n = 2172)	1-Year Probability of a Workers' Compensation Claim (n = 5966)	2-Year Probability of a Stroke, Myocardial Infarction, or Cardiovascular Procedure (n = 3099)
Proportion of days covered per 100, mean (SD), %	63.44 (31.40)	61.25 (31.71)	60.15 (31.73)	63.38 (31.38)	61.89 (31.35)
Age, mean (SD), y	52.53 (5.32)	52.62 (5.43)	52.58 (5.44)	52.56 (5.32)	52.15 (5.18)
Female sex, %	38.4	37.3	30.1	38.7	35.2
Annual salary, mean (SD), 1000s of \$	62.01 (51.18)	63.69 (55.52)	52.77 (32.78)	60.52 (50.49)	66.24 (49.56)
Emergency department visit in the 6 mo before the index date, %	7.8	9.8	11.8	7.8	7.5
Proportion of employees filling hypertension medications using mail order vs retail, %	18.1	22.9	25.2	18.1	23.8
Copayment per day supply, mean (SD), \$	0.43 (0.40)	0.47 (0.42)	0.49 (0.36)	0.43 (0.40)	0.48 (0.42)
No. of nonhypertension drugs, mean (SD)	6.19 (5.02)	6.14 (4.96)	5.79 (4.89)	6.16 (4.98)	5.92 (4.84)
Charlson Comorbidity Index, mean (SD)	0.64 (1.20)	0.65 (1.22)	0.67 (1.28)	0.64 (1.19)	0.58 (1.10)
Diabetes mellitus, %	23.5	23.7	23.9	23.4	24.1
Chronic heart failure, %	3.9	3.8	4.2	3.9	3.4
Myocardial infarction, %	2.2	2.3	2.3	2.1	0.7
Hyperlipidemia, %	48.3	49.8	48.6	47.9	51.0
Zip code first digit, % ^a					
0	9.9	6.7	6.0	10.0	6.9
1	9.6	4.6	6.7	10.0	4.3
2	9.2	7.5	8.7	9.2	7.2
3	15.3	15.7	23.2	15.7	13.0
4	4.2	4.0	6.4	4.3	4.1
5	2.0	2.3	4.1	2.0	2.2
6	3.4	3.7	4.1	3.5	3.4
7 [reference group]	29.5	36.4	25.3	30.1	40.6
8	8.0	9.5	9.4	8.0	9.2
9	8.9	9.6	6.3	7.1	9.1
Index month, %					
January	7.6	9.6	7.8	7.7	10.7
February	6.6	8.3	7.7	6.6	9.1
March	6.0	7.6	7.6	6.0	8.1
April	5.7	7.1	7.0	5.7	7.3
May	5.1	6.5	6.2	5.2	7.0
June	5.5	6.9	7.3	5.5	6.9
July	11.2	9.1	8.9	11.0	8.2
August	11.1	8.9	9.4	11.1	7.8
September	9.9	8.4	9.2	9.8	8.3
October	11.1	9.4	9.3	11.1	8.5
November	10.3	9.2	9.9	10.3	9.2
December [reference group]	10.0	9.1	9.8	10.1	9.0

^aPercentages may not add up to 100% due to rounding.

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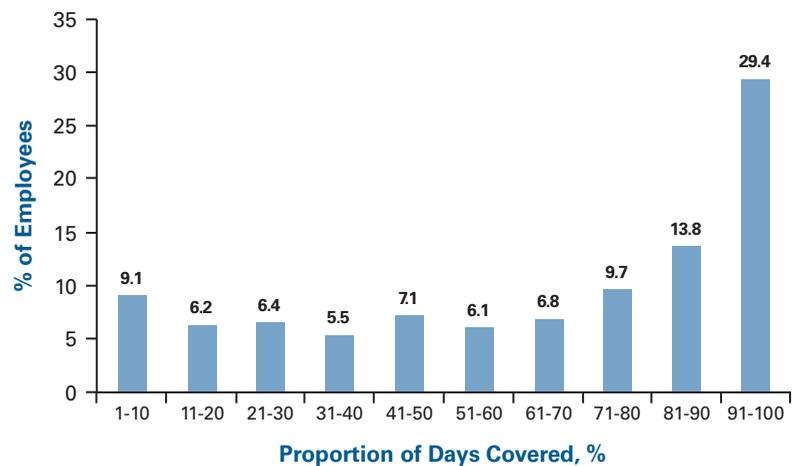
1 summarizes how the sample was obtained based on the eligibility requirements and the specific inclusion criteria. Out of 86,396 employees who met the hypertension diagnosis inclusion criterion shown in Table 1, only 7.2% met all other eligibility requirements and were included in the study cohort. Of 6236 employees, 1.3% (n = 84) had an emergency department visit with a primary diagnosis of hypertension, 3.7% (n = 228) had an inpatient admission with a primary diagnosis of hypertension, 0.4% (n = 25) had both an emergency department visit and an inpatient admission for hypertension, and the remaining 94.6% (n = 5899) had at least 2 outpatient medical claims (primary, secondary, and tertiary ICD-9-CM codes) for hypertension.

Table 2 gives demographic and basic medical service utilization statistics for the study cohort, as well as for the subcohorts used in the analysis of specific outcomes. The mean age of employees in the study cohort and subcohorts was approximately 52 years, the proportion of women varied between 30.1% and 38.7%, and the annual salary varied between \$52,000 and \$66,000, with the lowest salary in the subcohort with eligibility for the analysis of work absence days. The PDC among the different subcohorts varied between 60.2% and 63.4%. Between 7.5% and 11.8% of employees in the different subcohorts had emergency department visits in the 6 months before the index date. Between 18.1% and 25.2% of employees filled their hypertension medications using mail order versus retail. Copayment per day supply ranged from \$0.43 to \$0.49, and the number of nonhypertension drugs ranged from 5.8 to 6.2. The Charlson Comorbidity Index ranged from 0.58 to 0.67. Diabetes was present in 23.4% to 24.1% of employees in the various cohorts. Between 3.4% and 4.2% of employees had chronic heart failure, between 0.7% and 2.3% had a myocardial infarction, and between 47.9% and 51.0% had hyperlipidemia.

Hypertension-Related Drug Use

Among the employees in the study, the most commonly used medication class was antihypertensives (4508 employees [averaging 6.6 prescription claims per employee]). This was followed by diuretics (1596 employees [averaging 5.0 claims]), β -blockers (1350 employees [5.9 claims]), angiotensin-converting enzyme inhibitors (1252 employees [5.7 claims]), calcium channel blockers (1086 employees [5.7 claims]), and α -agonists or α -blockers (72 employees [4.4 claims]).

■ **Figure.** Distribution of Employees by Proportion of Days Covered for Hypertension-Related Medications



As shown in the Figure, 40.3% of the cohort had a PDC between 1% and 60%. Approximately 30.3% had a PDC between 61% and 90%. The remaining 29.4% of the cohort had a PDC above 90%.

Effect of PDC on Outcomes

Table 3 gives the estimated regression coefficients from the 9 pairs of models, and Table 4 summarizes the results of the analyses measuring the short-term effects of PDC on various adjusted medical and drug costs, medical service utilization, work absence days, and clinical outcomes. The results are provided separately for employees with high versus low prior medical costs.

In the group with low prior cost, there was a significant positive association between PDC and 3 of 9 measured outcomes, including annual medical and drug costs, annual hypertension-specific medical costs, and the annual number of work absence days. Specifically, a 10% increase in PDC was associated with 1.7% to 7.4% increases in these outcomes. In the group with high prior cost, PDC had varying effects. As PDC increased in this population, annual medical and drug costs, the annual number of inpatient hospital days, and the annual number of work absence days significantly decreased. For every 10% increase in PDC, the group with high prior cost could expect 5.1% less annual medical and drug costs, 8.2% fewer annual inpatient hospital days, and 12.5% fewer annual work absence days. However, annual hypertension-specific medical costs increased concomitantly with higher PDC among patients with high prior cost.

Among the control variables, the most influential were the following: (1) the number of nonhypertension drugs, which had statistically significant positive associations with outcomes variables in 10 of 18 models (Table 3); (2) the

■ **Table 3.** Estimated Regression Coefficients

Variable	Annual Medical and Drug Costs		Annual Hypertension-Specific Medical Costs		Annual No. of Medical Services		Annual No. of Inpatient Hospital Days		Annual No. of Work Absence Days	
	Low Prior Cost (n = 5950)	High Prior Cost (n = 286)	Low Prior Cost (n = 5950)	High Prior Cost (n = 286)	Low Prior Cost (n = 5950)	High Prior Cost (n = 286)	Low Prior Cost (n = 4729)	High Prior Cost (n = 213)	Low Prior Cost (n = 2082)	High Prior Cost (n = 90)
Intercept	6.7259	10.8189	4.7530	4.0982	2.5378	5.0269	-3.9794	3.5802	1.1668	3.0718
Proportion of days covered	0.0017	-0.0052	0.0040	0.0076	0.0000 ^a	0.0018 ^a	-0.0010 ^a	-0.0085	0.0071	-0.0134
Age	0.0205	-0.0375	—	—	—	-0.0171	0.0409	-0.0709	—	—
Female sex	-0.1651	0.2537	—	1.2315	—	—	—	0.6215	—	—
Annual salary	—	—	—	—	0.0005	—	—	—	-0.0130	—
Emergency department visit in 6 mo before the index date	0.1658	—	—	—	0.1051	—	0.3222	—	0.4271	—
Proportion of employees filling hypertension medications using mail order vs retail	—	—	-0.3100	—	—	—	-0.2992	0.8202	—	—
Copayment per day supply	—	—	—	—	—	—	—	—	—	—
No. of nonhypertension drugs	0.0828	0.0639	0.0192	—	0.0621	0.0556	0.0904	0.0956	0.1082	—
Charlson Comorbidity Index	0.2394	0.1864	—	—	0.2019	0.1458	0.2692	—	0.2311	—
Diabetes mellitus	-0.1936	-0.1612	—	-0.7989	-0.1020	—	-0.1189	—	-0.1773	—
Chronic heart failure	0.6098	—	0.7330	—	0.3528	0.2379	1.1537	0.9025	0.9595	—
Myocardial infarction	0.6519	—	0.8474	—	0.2420	—	1.3222	—	0.5646	—
Hyperlipidemia	—	—	—	—	0.1847	-0.3676	—	—	—	—
Zip code first digit										
0	—	—	—	—	—	—	—	—	—	—
1	0.2184	0.5258	0.2489	—	0.2824	0.3949	—	—	—	—
2	—	-0.6401	—	—	-0.0957	—	—	—	1.1606	—
3	—	—	—	—	—	—	0.3308	—	—	—
4	—	—	—	—	—	—	—	—	—	—
5	0.3780	—	0.4357	—	—	—	—	—	—	—
6	0.1769	0.7590	—	—	0.1377	—	0.5383	—	0.9076	—
8	—	—	—	—	—	—	—	—	—	—
9	0.2772	0.3692	0.3307	—	—	—	-0.3625	—	0.8066	—
Index month										
January	—	—	-0.2067	—	—	—	—	—	—	—
February	—	—	—	—	—	—	—	—	—	—
March	—	—	—	—	—	—	—	—	—	—
April	—	0.6910	—	—	—	—	—	—	—	—
May	—	—	—	—	—	—	—	—	—	—
June	—	—	-0.3683	—	—	—	—	—	—	—
July	0.1662	—	0.1718	—	—	—	—	—	—	—
August	0.1472	0.7958	—	1.3708	—	—	—	—	—	—
September	—	—	0.1907	—	—	-0.3940	0.4548	—	—	—
October	—	0.7040	—	—	—	—	—	—	—	—
November	0.1513	0.5685	—	—	—	—	—	—	—	—
Log likelihood for model's goodness of fit	42,341.60	3979.47	11,792.29	542.18	28,066.35	2091.68	-1116.51	65.79	1529.86	32.88

(Continued)

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Table 3. Estimated Regression Coefficients (*Continued*)

Variable	1-Year Probability of a Workers' Compensation Claim		2-Year Probability of a Stroke		2-Year Probability of a Myocardial Infarction		2-Year Probability of a Cardiovascular Procedure	
	Low Prior Cost (n = 5696)	High Prior Cost (n = 270)	Low Prior Cost (n = 2945)	High Prior Cost (n = 154)	Low Prior Cost (n = 2945)	High Prior Cost (n = 154)	Low Prior Cost (n = 2945)	High Prior Cost (n = 154)
Intercept	-1.5854	-3.2726	-7.8354	-7.5632	-4.4625	-3.2832	-6.4863	-4.2275
Proportion of days covered	0.0005 ^a	0.0102 ^a	0.0001 ^a	-0.0031 ^a	0.0000 ^a	-0.0136 ^a	0.0055 ^a	0.0058 ^a
Age	—	—	0.0788	0.1012	—	—	0.0498	—
Female sex	-0.3249	—	—	—	—	—	-1.4811	—
Annual salary	-0.0385	—	—	—	—	—	—	—
Emergency department visit in 6 mo before the index date	—	—	—	—	—	—	—	—
Proportion of employees filling hypertension medications using mail order vs retail	—	—	—	—	—	—	—	—
Copayment per day supply	—	—	—	—	—	—	—	—
No. of nonhypertension drugs	—	—	0.0452	—	—	—	0.0492	—
Charlson Comorbidity Index	—	—	0.2754	—	0.2438	—	0.2123	—
Diabetes mellitus	—	—	—	—	—	—	—	—
Chronic heart failure	—	—	—	—	—	—	—	—
Myocardial infarction	—	—	—	—	—	—	—	—
Hyperlipidemia	—	—	—	—	—	—	—	—
Zip code first digit								
0	—	—	—	—	—	—	—	—
1	—	—	0.8975	—	—	—	—	—
2	—	—	—	—	—	—	—	—
3	0.4706	—	0.6003	—	—	—	—	—
4	—	—	—	—	1.0552	—	—	—
5	—	—	—	—	—	—	—	2.8407
6	—	—	—	—	—	—	—	—
8	—	—	—	—	—	—	—	—
9	1.1797	—	—	—	—	—	—	—
Index month								
January	—	—	—	—	—	—	—	—
February	—	—	—	—	—	—	—	—
March	—	—	—	—	—	—	—	—
April	—	—	—	—	—	—	—	—
May	—	—	—	—	—	—	—	—
June	—	—	—	3.5510	—	—	—	—
July	—	—	—	—	0.8219	—	—	—
August	—	—	—	—	—	—	—	—
September	—	—	—	—	—	—	—	—
October	—	1.4934	—	—	—	—	—	—
November	—	—	—	—	—	—	—	—
Log likelihood for model's goodness of fit	-829.79	-33.86	-540.68	—	-234.66	-14.48	-399.15	-16.88

The dashes (—) indicate that the specific variable (age, salary, etc) was not statistically significant in the regression model and was removed from the model.

^aNot statistically significant ($P \geq .05$). All other estimates shown are statistically significant ($P < .05$).

■ **Table 4.** Effect of Proportion of Days Covered (PDC) on Outcomes

Outcome and Group	PDC, %					Change in Outcome Given a 10% Increase in PDC, %	P
	0	25	50	75	100		
Annual medical and drug costs, \$							
Low prior cost	4812	5020	5238	5466	5703	1.71	<.001 ^a
High prior cost	26,111	22,928	20,133	17,679	15,524	-5.07	.002 ^a
Annual hypertension-specific medical costs, \$							
Low prior cost	136	150	166	183	203	4.08	<.001 ^b
High prior cost	77	93	112	136	164	7.90	.02 ^a
Annual No. of inpatient hospital days							
Low prior cost	0.34	0.33	0.33	0.32	0.31	-1.00	.24
High prior cost	3.13	2.53	2.05	1.65	1.34	-8.15	.01 ^a
Annual No. of medical services							
Low prior cost	39.1	39.1	39.1	39.1	39.1	0.00	.97
High prior cost	117.5	112.3	107.4	102.6	98.1	-1.78	.22
Annual No. of work absence days							
Low prior cost	4.3	5.2	6.2	7.4	8.8	7.36	<.001 ^b
High prior cost	21.6	15.4	11.0	7.9	5.7	-12.54	.03 ^a
1-y Probability of a workers' compensation claim, %							
Low prior cost	2.00	2.03	2.05	2.07	2.10	0.45	.84
High prior cost	4.35	3.41	2.66	2.07	1.61	-9.49	.35
2-y Probability of a stroke, %							
Low prior cost	4.00	4.01	4.02	4.03	4.05	0.11	.97
High prior cost	10.59	9.87	9.20	8.57	7.97	-2.81	.70
2-y Probability of a myocardial infarction, %							
Low prior cost	1.44	1.44	1.45	1.45	1.45	0.02	>.99
High prior cost	3.62	2.60	1.86	1.33	0.95	-12.52	.44
2-y Probability of a cardiovascular procedure, %							
Low prior cost	1.78	2.04	2.33	2.67	3.05	5.54	.12
High prior cost	1.55	1.78	2.06	2.37	2.74	5.87	.71

^aSignificant at $P < .05$.
^bSignificant at $P < .001$.

Charlson Comorbidity Index (significant positive associations in 9 of 18 models); (3) chronic heart failure (significant positive associations in 7 of 12 models); (4) age (significant positive associations in 8 of 18 models; in the models for the subcohorts with low prior cost, the association of outcomes with age was positive, and in the models for the subcohorts with high prior cost [except for the model for myocardial infarction], the association of outcomes with age was negative);

(5) myocardial infarction (significant positive associations in 5 of 12 models); (6) sex (significant positive associations in 6 of 18 models; in the models for the subcohorts with low prior cost, the association of outcomes with female sex was negative, and in the models for the subcohorts with high prior cost, the association of outcomes with female sex was positive); and (7) diabetes (significant negative associations in 6 of 18 models).

DISCUSSION

This study measured the association of antihypertensive medication adherence with health benefit costs, medical service utilization, and work absence days. Among employees who were diagnosed as having hypertension and had low costs before the index date, PDC was associated with small but significant increases in healthcare costs and work absence days. Better adherence to hypertension-related medications was significantly associated with higher medical and drug costs, hypertension-specific medical costs, and the number of work absence days during the year following the index date. The effect of better adherence on other measured outcomes was not significant in this cohort with low prior cost, however.

Among employees with high prior cost, better adherence was significantly associated with lower healthcare costs and with fewer inpatient hospital days and work absence days. However, better adherence in this cohort was associated with significantly higher hypertension-specific medical costs. Although the effect of better adherence on other outcomes was not significant in this cohort, all other outcomes except for 2-year probability of a cardiovascular procedure tended to decrease as adherence increased.

The pattern of association of adherence with cost and hospitalization outcomes in the group with high prior cost is consistent with the results of an earlier study¹⁸ that demonstrated reductions in overall healthcare costs and hospitalization rates with increased drug utilization. The pattern of association observed in the group with low prior cost is a new finding. The earlier study did not divide the cohort by prior cost or health status but analyzed the total population with hypertension. In the present study, prior cost had a statistically significant effect on most outcomes measured and may be a proxy for severity of illness before diagnosis or treatment. Therefore, the observed difference in patterns of association of antihypertensive medication adherence with most outcomes between cohorts with low versus high prior costs is not surprising.

The association between PDC and significant health events did not show the expected pattern based on the literature's indications that pharmacologic treatment of hypertension reduces the risk of stroke, coronary events, and heart failure.^{9,11-17} A 2-year time frame may be inadequate to measure the effect of better hypertension management. Also, because the measurement approach assessed adverse health events in much the same period as medication adherence, the positive association between PDC and event likelihood could, in some cases, reflect a sudden increase in compliance following a frightening medical problem. Furthermore, this study did not

permit the analysis of clinical variables such as blood pressure readings.

Study Strengths

This study adds to the literature on the association between medication adherence and medical and drug costs, health service utilization, and clinical outcomes by measuring more outcomes than prior studies. These include the number of work absence days, the number of inpatient hospital days, and the number of medical services, as well as probabilities of workers' compensation claims, stroke, myocardial infarction, and cardiovascular procedures.

Study Limitations

The study cohort and subcohorts were defined based on retrospective medical and drug claims data; therefore, causal relationships between adherence and outcomes cannot be presumed in this study. Also, there are some inherent drawbacks to the use of medical claims data when measuring medical service utilization and medical and drug costs such as the possibility that ICD-9-CM codes on medical claims do not accurately reflect a patient's diagnosis. Finally, the lack of information about an employee's duration of hypertension or severity is a limitation of retrospective analyses. There is evidence that the severity of hypertension is an influential factor when evaluating the effect of PDC on outcomes.³⁷ Unfortunately, the data did not include reliable indicators of blood pressure readings to control for hypertension severity when measuring the effect of PDC.

CONCLUSIONS

Medication adherence was associated with improvement in some short-term utilization measures among high-prior-cost employees. However, significant short-term improvement was not seen among low-prior-cost employees.

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