

Does Medication Adherence Lead to Lower Healthcare Expenses for Patients With Diabetes?

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Objectives: To examine the relationship between medication adherence and healthcare outcomes and expenses and to investigate whether the duration of type 2 diabetes mellitus (T2DM) has a role in the aforementioned relationship.

Data Source/Study Setting: Health insurance claims data under a universal coverage system in Taiwan.

Study Design: Seven years of longitudinal analysis was performed to examine the association between medication adherence of oral antihyperglycemic drugs and outcomes among patients with newly diagnosed T2DM. Generalized estimating equations were conducted to assess the temporal relationship while controlling for unobserved characteristics of patients.

Results: Better medication adherence was associated with decreased hospitalization and emergency department (ED) visits for diabetes or related conditions. The results also revealed that medication adherence was negatively associated with the expenses of hospitalization and ED visits for diabetes or related conditions, but medication adherence was positively associated with patients' total healthcare expenses. However, the adherence-related differences in total healthcare expenses began to decrease 5 years after the time of diabetes onset.

Conclusions: Adherence to medication can improve healthcare outcomes but is associated with higher total healthcare expenses, especially during the years immediately following the onset of diabetes. Long-term follow-up is needed for further investigation.

Am J Manag Care. 2013;19(8):662-670

For author information and disclosures, see end of text.

Diabetes is a prevalent health condition that is associated with significant morbidity and mortality.¹ In Taiwan and other countries, the prevalence and incidence of diabetes have been increasing over the past decade.²⁻⁴ This increase imposes a substantial economic burden on the healthcare system.^{5,6} Improving glycemic control may delay the onset and hamper the progression of macrovascular and microvascular complications associated with diabetes.⁷ Long-term glycemic control can be effectively managed through dietary control and lifestyle changes, but adherence to prescribed medication is the most influential aspect of diabetes management.⁸

An improvement in medication adherence may lead to better glycemic control,⁹ which, in turn, may reduce complications and healthcare utilization, such as the likelihood of hospitalization and emergency department (ED) visits. Asche et al (2011) summarized the findings of empirical studies and concluded that better medication adherence is associated with improved glycemic control and decreased healthcare service utilization.¹⁰ In addition, several researchers have reported that increasing adherence to oral antihyperglycemic medications may actually increase the expenses of these medications¹¹⁻¹³ and decrease the expenses for other healthcare services, such as expenses for diabetes-related hospitalizations or ED visits.¹¹⁻¹³ However, whether the higher drug expenses would be offset by the reduction in healthcare expenses of other healthcare services is still controversial.^{10,14}

The present study adds to the growing body of literature in 3 ways. First, most of the studies use observational designs which are subject to the problem of endogeneity, due to the healthy user effect¹³ or healthy adherer bias.¹⁵ If certain observed or unobserved characteristics of patients are related to both the medication adherence and their outcomes and expenses of healthcare services, then the characteristics may bias the result of the study. A typical example is that patients who are adherent to their medications are healthier and are more likely to adopt a healthy lifestyle, which may result in lower healthcare utilization and expenses irrespective of the effects of medication adherence. This study employed a multi-year longitudinal design to account for unobserved time-invariant characteristics of patients and to ensure the temporality of the association.¹⁶

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Furthermore, in the sensitivity analysis section, we used a propensity score matching (PSM) approach to reduce the potential differences in the observed characteristics of patients between the adherent group and the nonadherent group for minimizing possible selection bias.¹⁷

Second, the majority of previous studies have only conducted short-term follow-up analyses.^{11,12,18-21} Therefore, there is limited evidence regarding the long-term effects of adherence to oral antihyperglycemic medications on the outcomes and expenses of healthcare.^{22,23} A longitudinal design may clarify whether medication adherence has different effects on healthcare expenses during the different duration of diabetes, which is currently unknown. Finally, this study focused on newly diagnosed patients only; therefore, the results might exclude the cumulative effects of adherence that occurred prior to the study period. A similar sample selection was used by Hong and Kong (2011).²³

Medication adherence is closely associated with the healthcare system. The majority of studies concerning the relationship between medication adherence and the outcomes and expenses of healthcare have been conducted in the United States. Existing evidence shows that higher prescription cost-sharing reduces medication adherence, due to financial barriers.^{24,25} In recent years, a number of employers have implemented the policy of value-based insurance design (VBID). This policy encourages medication adherence for patients with chronic diseases by reducing their medication copayment.²⁶

Taiwan's National Health Insurance (NHI) program was launched in 1995 and provides a comprehensive benefits package to the public with a low drug cost-sharing requirement.²⁷ The outpatient prescription drug copayment was either zero or up to US\$6, depending on the expenses of the prescribed medication for each physician visit (in 2009, NT\$33 = US\$1). Financial barriers to accessing prescribed medications should only be a minor concern in Taiwan compared with in the United States. Therefore, medication adherence in Taiwan should be less confounded by the ability of patients to afford the medication. Through the use of a longitudinal study design, this study aimed to examine the relationship between medication adherence and healthcare outcomes and expenses for adult patients with newly diagnosed type 2 diabetes mellitus (T2DM). Furthermore, this study also examined whether the duration of diabetes may play a role in the aforementioned relationship.

Take-Away Points

The present study uses a longitudinal design to examine the relationship between medication adherence and healthcare outcomes and expenses, and to investigate whether the duration of type 2 diabetes mellitus has a role in the aforementioned relationship for patients with newly diagnosed diabetes.

- Better medication adherence was associated with favorable healthcare outcomes.
- Better medication adherence was associated with decreased expenses of hospitalization and emergency department visits for diabetes-related conditions, but was associated with higher total healthcare expenses.
- However, the adherence-related differences in total healthcare expenses began to decrease 5 years after the time of diabetes onset.

METHODS

Data and Study Sample

The NHI claim data set for this study was obtained from the National Health Research Institutes of Taiwan. Using the NHI claims data set from 1999 to 2009, we identified patients with T2DM by ICD-9-CM codes 250.xx while excluding type 1 diabetes mellitus codes 250.x1 and 250.x3.²⁸ New patients with T2DM were identified by lacking T2DM-related claims during 1999 and 2001, before the index date (the date of the first claim with the diagnosis of T2DM for each patient) of diagnosis in 2002. Patients were included in the analysis if they: (1) were at least 18 years old on the index date; (2) had a prescription for oral antihyperglycemic medications at the index date of initial diagnosis to capture the appropriate timing of initial prescriptions for new patients, as done in previous studies²³; (3) had at least 1 prescription for oral antihyperglycemic medications after the second year during the study period to ensure that patients who were in the study required ongoing pharmacologic therapy; and (4) had no insulin prescriptions during any of the years in the study period because the claims data did not provide sufficient information about the insulin regimen of each patient, such as the use of a sliding-scale insulin regimen, as employed in a previous study.¹⁸ We compiled baseline information from the first year following initial diagnosis of T2DM, and we subsequently collected follow-up information for each patient over the subsequent 6 years in the analysis. As a result, a total of 11,580 patients and 69,480 patient-years were included in the analysis. The unit of analysis was patient-years.

Measures

Dependent Variables. The dependent variables were healthcare outcomes and healthcare expenses. Healthcare outcomes were based on whether the patient was hospitalized or had an ED for diabetes or cardiovascular/cerebrovascular conditions during each year of the study period; the definition has been used by Lau and Nau (2004).¹⁸ Three variables

were used to measure healthcare expenses: expenses associated with oral antihyperglycemic medications, expenses for hospitalization or ED visits due to diabetes or cardiovascular/cerebrovascular conditions, and total healthcare expenses for all conditions incurred by the patients. Total healthcare expenses included expenses for ambulatory care, ED visit, hospitalization, laboratory tests, pharmaceuticals, and patient's copayment. The healthcare expenses were adjusted for inflation by using the consumer price index to facilitate the comparison of figures from various years with those from 2009.

Independent Variables. The independent variables that we included in the analysis consisted of adherence to medications, the duration of diabetes, and the interaction of the duration and adherence to medications. Adherence to medications was measured using the medication possession ratio (MPR) which was based on filled prescriptions for 7 oral antihyperglycemic medications. According to the ATC (Anatomical Therapeutic Chemical) code, these medications included biguanides (A10BA), sulfonamides or urea derivatives (A10BB), combinations of oral blood glucose-lowering drugs (A10BD), alpha glucosidase inhibitors (A10BF), thiazolidinediones (A10BG), dipeptidyl peptidase 4 (DPP-4) inhibitors (A10BH), and other blood glucose-lowering drugs, excluding insulin (A10BX).

In this study, the MPR was calculated as the ratio of the number of days of prescribed medication divided by the total number of days in each study year. Refilled medication days for oral antihyperglycemic medications were also included. The days when patients were prescribed oral antihyperglycemic medications during a hospital stay were excluded from the denominator in the MPR calculation. In addition, patients might receive multiple medications for different numbers of days during a visit; the number of the longest days of the prescribed medications (usually for chronic conditions such as diabetes) in a visit is reported in the NHI claims data. Patients were considered to be adherent to oral antihyperglycemic medications if the MPR was equal to or larger than 80%. This cutoff point has been widely used in previous studies to categorize medication adherence.^{18,19,21,23}

In addition, the duration of diabetes was divided into 2 categories: less than 5 years (the second to fourth year after the initial diagnosis) and 5 years or more (the fifth to seventh year after the initial diagnosis). Effect modification for the duration of diabetes was examined by the inclusion of an interaction term for medication adherence and the duration of diabetes.

Covariates

Several confounding factors were controlled for in the regression models, including yearly time-dependent variables

and time-independent variables. The time-dependent variables in these models included the characteristics of patients and healthcare providers. The characteristics of patients included age, sex, number of physician visits, hospitalizations in the previous year, diabetes complication severity index (DCSI),²⁹ chronic illness with complexity (CIC) index,³⁰ intensity of the diabetes drug regimen, the average number of medications per prescription, and enrollment in the NHI diabetes pay-for-performance (P4P) program.^{31,32}

The DCSI contained 7 categories of complications: cardiovascular complications, nephropathy, retinopathy, peripheral vascular disease, stroke, neuropathy, and metabolic disorders. The CIC index was used to adjust for comorbidity of patients with multiple chronic diseases. This index contained information regarding non-diabetes physical illness complexity (including cancers, as well as gastrointestinal, musculoskeletal, and pulmonary diseases), diabetes-related complexity, microvascular complications, and mental illness/substance abuse complexity. We excluded diabetes-related complexity to avoid the duplication of the comorbidity effect presented by the DCSI index. In the analysis, we counted the number of comorbidities based on the CIC. The intensity of the diabetes drug regimen was indicated whether study subjects used oral monotherapy or oral combination therapy. The average number of medications per prescription was stratified by the mean number of medications per prescription (≥ 3 medications, < 3 medications). The healthcare provider characteristics included the accreditation level of the hospital most frequently visited for diabetes care (medical center, regional hospitals, district hospitals, clinics)³³ and specialty of the physician most frequently seen for diabetes care (metabolism endocrinologist, others). The time-independent variable was the subject's sex.

Statistical Analysis. Generalized estimating equations (GEEs) were used with various proper distributions. The analysis accounted for the intraclass correlation between repeated observations of the same subject.^{16,34} Based on the characteristics of the variables used herein, the likelihood of hospitalization and ED visits was analyzed using a binominal distribution. Additionally, values from the healthcare expenses were skewed to the right. Therefore, we used the GEE model with a logarithmic link function and a gamma distribution to analyze the skew of the healthcare expense data. A similar approach has been used in the econometric literature to assess healthcare costs.³⁵

In addition to these models, we conducted 3 sensitivity analyses to improve the robustness of this study. First, the diabetes and cardiovascular/cerebrovascular-related hospitalizations was originally based on Lau and Nau's definition (2004).¹⁸ Because this definition only includes specific aspects of health conditions that are related to diabetes, we may have underesti-

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■ Table 1. Baseline Characteristics of Study Subjects in the Year Being Diagnosed With Type 2 Diabetes Mellitus (N = 11,580)

Variables	N	%
Total	11,580	100
Sex		
Male	6141	53.03
Female	5433	46.92
Missing	6	0.05
Age, y (mean ± SD)	55.56	11.25
Age groups, y		
18-44	2011	17.37
45-64	7035	60.75
65+	2534	21.88
Number of physician visits (mean ± SD)	23.77	15.38
Number of ambulatory care visits by tertiles		
Low	2627	22.69
Intermediate	4399	37.99
High	4554	39.33
DCSI score		
Score 0	7067	61.03
Score 1	2722	23.51
Score 2+	1791	15.47
CIC index count		
0	4361	37.66
1	4467	38.58
2+	2752	23.77
Hospitalization in the previous year	1827	15.78
Multiple oral antihyperglycemic medications	6062	52.35
Number of medications per prescription (mean ± SD)	3.49	1.29
Number of medications per prescription ≥3	7162	61.85
Enrolled P4P program	697	6.02
Accreditation of hospitals		
Medical center	2176	18.79
Regional hospitals	2847	24.59
District hospitals	2241	19.35
Clinics	4316	37.27
Metabolism endocrinologist	260	2.25

CIC index count indicates chronic illness with complexity index count; DCSI, diabetes complication severity index; P4P, pay-for-performance; SD, standard deviation.

mated or overestimated the results of our study. Therefore, we examined the effects of medication adherence on healthcare outcomes and expenses based on more general definitions of diabetes-related conditions, including the definitions made by Sokol et al (2005)¹² and Bethel et al (2007)¹. Second, we used various MPR cut-off points to examine the stability of the association between MPR and healthcare outcomes as well as

expenses. Finally, because the patients with diabetes were not randomly assigned to the medication-adherent group or non-adherent group, we used a PSM approach to minimize the selection bias and assigned patients with diabetes to the non-adherent group.¹⁷ We employed the caliper matching method (also known as the greedy algorithm) with 1-to-1 matching between the adherent and nonadherent groups based on the

■ **Table 2.** Interest Variables According to the Year

Variables	Year 1		Year 2		Year 3	
	N	%	N	%	N	%
Medication adherence						
MPR (mean ± SD)	75.21	33.01	75.14	28.68	80.85	25.94
MPR ≥80%	6379	55.09	6424	55.47	7351	63.48
Healthcare outcomes						
Hospitalization for DM or cardiovascular/cerebrovascular-related conditions	1047	9.04	972	8.39	983	8.49
ED visits for DM or cardiovascular/cerebrovascular-related conditions	724	6.25	625	5.40	625	5.40
Healthcare expenses (mean ± SD)						
Drug expenses for oral antihyperglycemic medications	3609	4154	4459	5246	5358	5870
Expenses of hospitalizations and ED visits for DM or cardiovascular/cerebrovascular-related conditions	5335	29,405	5396	29,845	5984	34,916
Total healthcare expenses for any condition	34,490	45,929	36,350	46,535	39,004	51,421

DM indicates diabetes mellitus; ED, emergency department; MPR, medication possession ratio; SD, standard deviation.

propensity score. A total of 7728 patients and 46,368 patient-years were included in the matched analysis. The analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, North Carolina) and Stata 9.1 (Stata Corp, College Station, Texas).

RESULTS

Descriptive Findings

Table 1 presents the baseline characteristics of the study subjects in the year being diagnosed with T2DM. In terms of basic characteristics, the mean age of subjects was 55.56 years. The average number of physician visits for any condition in the previous year was 23.77 and the rate of hospitalization in the previous year was 15.78%. Approximately 61.03% of the study sample had a DCSI score of 0, whereas 15.47% had a score of 2 or higher. In addition, 61.85% of the study sample had an average of more than 3 medications per prescription.

Table 2 presents the trends for interest variables. The average MPR slightly decreased from 75.21% in the first year after diagnosis of diabetes to 75.14% in the second year and then increased in the subsequent years to 88.87% in the last year of the study period. The proportion of patients who were considered to be adherent to oral antihyperglycemic medications (MPR ≥80%) increased during the study period. The rates of hospitalization for diabetes or cardiovascular/cerebrovascular conditions decreased from 9.04% in the first year after diagnosis of diabetes to 8.39% in the second year, respectively. These rates then increased in the subsequent years to 11.74% in the last year of the study period. The rate of ED visits for diabetes or cardiovascular/cerebrovascular conditions decreased from 6.25% in the first year to 5.40% in the second and third year and then increased steadily during the subsequent years. Ad-

ditionally, the mean drug expenses for oral antihyperglycemic medications, the average expenses for diabetes or cardiovascular/cerebrovascular-related hospitalizations and ED visits, and total healthcare expenses increased during the study period.

Relationship Between Medication Adherence and Healthcare Outcomes

Table 3 presents the results of the GEE models concerning the relationship between medication adherence and healthcare outcomes. The first model examined the relationship between medication adherence and healthcare outcomes (Model 1). In the second model (Model 2), the interaction of medication adherence and the duration of diabetes was incorporated. In Model 1, patients with better medication adherence were less likely to be hospitalized for diabetes or cardiovascular/cerebrovascular-related conditions (odds ratio [OR] = 0.74, 95% confidence interval [CI] = 0.69-0.78). Similarly, patients with better medication adherence were less likely to have ED visits for diabetes or cardiovascular/cerebrovascular-related conditions based on Model 1 (OR = 0.78, 95% CI = 0.73-0.84). In Model 2, the interaction term revealed that the duration of diabetes significantly moderated the relationship between medication adherence and hospitalization (OR = 0.86, 95% CI = 0.76-0.97) but did not moderate the relationship between medication adherence and ED visits (OR = 0.91, 95% CI = 0.79-1.05).

Relationship Between Medication Adherence and Healthcare Expenses

Results from the GEE models concerning the relationship between adherence and healthcare expenses are presented in **Table 4**. Patients in the adherent group had higher drug expenses

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Year 4		Year 5		Year 6		Year 7	
N	%	N	%	N	%	N	%
84.22	24.20	86.55	22.72	88.30	22.15	88.87	22.94
7966	68.79	8481	73.24	8852	76.44	8997	77.69
969	8.37	1049	9.06	1129	9.75	1359	11.74
692	5.98	719	6.21	777	6.71	864	7.46
6022	6333	6468	6740	6689	7050	7272	7451
5706	32,813	6543	36,447	7261	39,185	11370	59,076
38,666	47,398	40,546	53,424	42,087	59,637	48,348	78,985

for oral antihyperglycemic medications than did patients in the nonadherent group ($\beta = 0.52, P < .001$). However, patients in the adherent group had lower expenses for hospitalizations and ED visits for diabetes or cardiovascular/cerebrovascular-related conditions than did patients in the nonadherent group ($\beta = -0.56, P < .001$). The results indicated that adherence to oral antihyperglycemic medications was positively associated with total healthcare expenses for any condition ($\beta = 0.09, P < .001$). In

addition, we found that the duration of diabetes moderated the relationship between medication adherence and total healthcare expenses ($\beta = -0.16, P < .001$). These results indicated that during the 4 years following diagnosis, patients who had good medication adherence tended to have higher healthcare expenses than patients who had poor medication adherence. However, this relationship was attenuated at 5 years after initial diabetes diagnosis.

Sensitivity Analyses. First, while using the definitions made by Sokol et al (2005)¹² and Bethel et al (2007)¹, we found the results were similar to those obtained by using the definition of Lau and Nau (2004)¹⁸ (eAppendix A Table 1-1 and Table 1-2). Second, while using various cut-off points for MPR (70% and 90% respectively), we found stable results concerning the association between MPR and healthcare outcomes and expenses (eAppendix B Table 2-1 and Table 2-2). Finally, the PSM process yielded a new study sample with similar distribution of the characteristics between the adherent and nonadherent groups, and generated estimates similar to the original regression models (eAppendix C Table 3-1 and Table 3-3). In summary, these sensitivity analyses indicated that the results from the study were robust.

Table 3. GEE Regression Analysis of Medication Adherence and Healthcare Outcomes

Variables	Model 1			Model 2		
	OR	95% CI		OR	95% CI	
Hospitalization for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: non-adherence [MPR <80%])	0.74	0.69	0.78	0.79	0.73	0.86
Duration of 5 years or more (reference group: less than 5 years)	1.28	1.21	1.35	1.42	1.29	1.57
Interaction between medication adherence and duration of DM	—	—	—	0.86	0.76	0.97
ED visits for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <80%])	0.78	0.73	0.84	0.82	0.74	0.91
Duration of 5 years or more (reference group: less than 5 years)	1.25	1.18	1.34	1.34	1.19	1.51
Interaction of medication adherence and duration of DM	—	—	—	0.91	0.79	1.05

CI indicates confidence interval; CIC index count, chronic illness with complexity index count; DCSI, diabetes complications severity index; DM, diabetes mellitus; ED, emergency department; GEE, generalized estimation equation; MPR, medication possession ratio; OR, odds ratio; P4P, pay-for-performance.

All models were controlled for sex, age groups, number of physician visits by tertiles, DCSI score, CIC index count, hospitalization in the previous year, intensity of the DM drug regimen, number of medications per prescription ≥ 3 , enrollment in the P4P program, accreditation level of the hospital most frequently visited for diabetes care, and specialty of the physician most frequently seen for diabetes care.

■ **Table 4.** GEE Regression Analysis of Medication Adherence and Healthcare Expenses

Variables	Model 1			Model 2		
	β	SE	P	β	SE	P
Drug expenses for oral antihyperglycemic medications						
Adherence (reference group: nonadherence [MPR <80%])	0.52	0.01	<.001	0.55	0.01	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.12	0.00	<.001	0.17	0.01	<.001
Interaction between medication adherence and duration of DM	—	—	—	-0.07	0.01	<.001
Expenses for hospitalizations or ED visits for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <80%])	-0.56	0.08	<.001	-0.43	0.10	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.56	0.07	<.001	0.78	0.12	<.001
Interaction between medication adherence and duration of DM	—	—	—	-0.31	0.14	.028
Total healthcare expenses for any condition						
Adherence (reference group: nonadherence [MPR <80%])	0.09	0.01	<.001	0.16	0.02	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.13	0.01	<.001	0.25	0.02	<.001
Interaction between medication adherence and duration of DM	—	—	—	-0.16	0.02	<.001

CIC index count indicates chronic illness with complexity index count; DCSI, diabetes complication severity index; DM, diabetes mellitus; ED, emergency department; GEE, generalized estimation equation; MPR, medication possession ratio; P4P, pay-for-performance; SD, standard deviation; SE, standard error.

All models were controlled for sex, age group, number of physician visits by tertiles, DCSI score, CIC index count, hospitalization in the previous year, intensity of the DM drug regimen, number of medications per prescription ≥ 3 , enrollment in the P4P program, accreditation level of the hospital most frequently visited for diabetes care, and specialty of the physician most frequently seen for diabetes care.

DISCUSSION

The objectives of this study were to examine the association between medication adherence and healthcare outcomes and expenses using a longitudinal study design. The results indicated that better medication adherence was associated with decreased hospitalizations and ED visits for diabetes or cardiovascular/cerebrovascular-related conditions. We also found that medication adherence was negatively associated with healthcare expenses that were due to diabetes or cardiovascular/cerebrovascular-related hospitalizations and ED visits, but it was positively associated with the patient's total healthcare expenses. Nevertheless, the adherence-related differences in total healthcare expenses were observed to decrease beginning 5 years after the onset of diabetes.

Our findings support previous studies suggesting that there is a significant association between medication adherence and decreased hospitalizations^{11,12,18-20,23} and ED visits.¹¹ Medication adherence may lead to better glycemic control,⁹ which further reduces the need for hospitalizations and ED visits by decreasing the incidences of microvascular and macrovascular complications. Moreover, we found that the relationship between better medication adherence and decreased hospitalizations was stronger a certain number of years after the onset of diabetes. Given the chronic nature of diabetes, the duration of diabetes has been an increased risk of the development

of complications, such as microalbuminuria³⁶ and cardiovascular events.³⁷ A longer follow-up study is needed to further explore the relationship between medication adherence and the occurrence of complications.

Consistent with most previous studies, we found that higher medication adherence was associated with increased drug expenses¹¹⁻¹³ but was also associated with lower diabetes-related hospitalization or ED visit expenses.¹¹⁻¹³ Studies regarding the effects of adherence to oral antihyperglycemic medications on total healthcare expenses are limited, and the results tend to be inconclusive.^{10,14} Some studies have found that increased medication adherence is associated with lower total healthcare expenses,^{12,21-23} while others have found the opposite relationship.^{11,20} Our study found that better medication adherence was associated with increased total healthcare expenses. This result implies that reduced expenses for diabetes-related hospitalizations and ED visits did not offset the higher expenses associated with oral antihyperglycemic medications or physician visits. A potential explanation for this is that because of the high accessibility to healthcare, the low cost-sharing for patients, and the fee-for-service reimbursement for physicians in Taiwan, patients are typically prescribed medications for fewer days than they need and thus are required to make a return visit to the physician. The higher expenses associated with physician visits significantly contributed to the increased total expenses for patients who had better medication adherence. However, the positive rela-

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relationship between medication adherence and total healthcare expenses was attenuated after 5 years following the onset of diabetes. Therefore, the effects of medication adherence may be more pronounced with longer duration of diabetes. A longer follow-up study and further exploration are needed.

Previous studies in the United States have found that a higher level of prescription drug cost-sharing was associated with lower medication adherence.^{24,25} In the present study, the mean value of MPR for patients with newly diagnosed diabetes ranged from 75.21 to 88.87% throughout the study period. An MPR of 80% is frequently considered to indicate good adherence for patients.³⁸ The mean value of MPR in Taiwan was higher than that in some studies conducted in other countries, such as the United States⁹ and Korea.²³ This difference may be due to Taiwan's universal health insurance, which provides comprehensive medication coverage and involves a low drug cost-sharing requirement. However, we found that variation in MPR values still exists in a setting with low drug cost-sharing, which is similar to VBID in the United States. We suggest that non-financial barriers to medication adherence might also be important for improving medication adherence for patients with diabetes. Increasing the patients' health literacy (such as their awareness of the importance of adherence), enhancing the continuity of care between physicians and patients, and the development of a pay-for-performance program to promote medication adherence are some strategies for healthcare policy makers to consider.

It should be noted that the present study has limitations. First, this study did not include some unobserved (such as health literacy) or unavailable characteristics (such as socioeconomic status, severity of illness) in the regression models. Some of these characteristics might influence both medication use and their healthcare outcomes and expenses. For example, patients with a higher education level might be more compliant and would have better healthcare outcomes and lower healthcare expenses, which might result in an overestimation of the effects of medication adherence. Nevertheless, this study employed a longitudinal study design which might account for the unobserved time-invariant characteristics, and this concern might be mitigated. In addition, we included several proxy indicators for severity of illness in the regression models, namely DCSI score, CIC index count, number of physician visits, and hospitalization in the previous year, which might also lessen the bias due to confounders not incorporated in the model. Second, the determination of medication adherence using claims data may have resulted in an overestimation of medication adherence, although MPR calculation based on claims data is a common measure in the literature for quantifying medication adherence.^{11,12,18-23} Third, due to the lack of information, this study did not incorporate more appropriate outcome mea-

asures for diabetes care, such as A1C levels. Finally, there are certain unique aspects of Taiwan's healthcare system that may make it difficult to generalize the results of this study to other populations.

In conclusion, the findings of this study suggest that adherence to medications can reduce the risk of hospitalizations and ED visits and can lower healthcare expenses for diabetes-related hospitalizations and ED visits. While patients with better medication adherence still incur higher total healthcare expenses, the adherence-related differences in total healthcare expenses seem to decrease beginning 5 years after the onset of diabetes. The long-term effects of medication adherence deserve further investigation.

Acknowledgment

The study was supported by grants from the National Science Council (NSC100-2410-H-002-084) and the National Health Research Institute (NHRI-EX102-10225PI) in Taiwan. The funding source had no role in the study.

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Funding Source: None.

Author Disclosures: The authors (S-HC, C-CC, C-HT) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (S-HC); acquisition of data (S-HC); analysis and interpretation of data (S-HC, C-CC, C-HT); drafting of the manuscript (S-HC); critical revision of the manuscript for important intellectual content (S-HC, C-HT); statistical analysis (C-CC); obtaining funding (S-HC); and supervision (S-HC).

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REFERENCES

1. Bethel MA, Sloan FA, Belsky D, Feinglos MN. Longitudinal incidence and prevalence of adverse outcomes of diabetes mellitus in elderly patients. *Arch Intern Med.* 2007;167(9):921-927.
2. Fox CS, Pencina MJ, Meigs JB, Vasan RS, LevitzkyYS, D'Agostino RB Sr. Trends in the incidence of type 2 diabetes mellitus from the 1970s to the 1990s: the Framingham Heart Study. *Circulation.* 2006;113(25):2914-2918.
3. Tseng CH, Tseng CP, Chong CK, et al. Increasing incidence of diagnosed type 2 diabetes in Taiwan: analysis of data from a national cohort. *Diabetologia.* 2006;49(8):1755-1760.
4. Chang HY, Hsu CC, Pan WH, et al. Gender differences in trends in diabetes prevalence from 1993 to 2008 in Taiwan. *Diabetes Res Clin Pract.* 2010;90(3):358-364.
5. American Diabetes Association. Economic costs of diabetes in the U.S. in 2007. *Diabetes Care.* 2008;31(3):596-615.
6. Bureau of National Health Insurance. The 2009 report of National Health Insurance Annual Statistical report, 2010 [in Chinese].
7. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ.* 2000;321(7258):405-412.
8. Hearnshaw H, Lindenmeyer A. What do we mean by adherence to treatment and advice for living with diabetes? a review of the literature on definitions and measurements. *Diabet Med.* 2006;23(7):720-728.

9. Cramer JA. A systematic review of adherence with medications for diabetes. *Diabetes Care*. 2004;27(5):1218-1224.
10. Asche C, LaFleur J, Conner C. A review of diabetes treatment adherence and the association with clinical and economic outcomes. *Clin Ther*. 2011;33(1):74-109.
- Hepke KL, Martus MT, Share DA. Costs and utilization associated with 11. pharmaceutical adherence in a diabetic population. *Am J Manag Care*. 2004;10(2, pt 2):144-151.
12. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43(6):521-530.
13. Roebuck MC, Liberman JN, Gemmill-Toyama M, Brennan TA. Medication adherence leads to lower health care use and costs despite increased drug spending. *Health Aff*. 2011;30(1):91-99.
14. Salas M, Hughes D, Zuluaga A, Vardeva K, Lebmeier M. Costs of medication nonadherence in patients with diabetes mellitus: a systematic review and critical analysis of the literature. *Value Health*. 2009;12(6):915-922.
15. Stuart B, Davidoff A, Lopert R, Shaffer T, Samantha Shoemaker J, Lloyd J. Does medication adherence lower Medicare spending among beneficiaries with diabetes? *Health Serv Res*. 2011;46(4):1180-1199.
16. Stock JH, Watson MW. *Introduction to Econometrics*. Boston: Addison Wesley; 2003.
17. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55.
18. Lau DT, Nau DP. Oral antihyperglycemic medication nonadherence and subsequent hospitalization among individuals with type 2 diabetes. *Diabetes Care*. 2004;27(9):2149-2153.
19. Ho PM, Rumsfeld JS, Masoudi FA, et al. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med*. 2006;166(17):1836-1841.
20. Karve S, Cleves MA, Helm M, Hudson TJ, West DS, Martin BC. An empirical basis for standardizing adherence measures derived from administrative claims data among diabetic patients. *Med Care*. 2008;46(11):1125-1133.
21. Hansen RA, Farley JF, Droege M, Maciejewski ML. A retrospective cohort study of economic outcomes and adherence to monotherapy with metformin, pioglitazone, or a sulfonylurea among patients with type 2 diabetes mellitus in the united states from 2003 to 2005. *Clin Ther*. 2010;32(7):1308-1319.
22. Balkrishnan R, Rajagopalan R, Camacho FT, Huston SA, Murray FT, Anderson RT. Predictors of medication adherence and associated health care costs in an older population with type 2 diabetes mellitus: a longitudinal cohort study. *Clin Ther*. 2003;25(11):2958-2971.
23. Hong JS, Kang HC. Relationship between oral antihyperglycemic medication adherence and hospitalization, mortality, and healthcare costs in adult ambulatory care patients with type 2 diabetes in South Korea. *Med Care*. 2011;49(4):378-384.
24. Gibson TB, Song X, Alemayehu B, et al. Cost sharing, adherence, and health outcomes in patients with diabetes. *Am J Manag Care*. 2010;16(8):589-600.
25. Gu Q, Zeng F, Patel BV, Tripoli LC. Part D coverage gap and adherence to diabetes medications. *Am J Manag Care*. 2010;16(12):911-918.
26. Chernew ME, Rosen AB, Fendrick AM. Value-based insurance design. *Health Aff*. 2007;26(2):w195-w203.
27. Cheng TM. Taiwan's new national health insurance program: genesis and experience so far. *Health Aff (Millwood)*. 2003;22(3):61-76.
28. Lin CC, Lai MS, Syu CY, Chang SC, Tseng FY. Accuracy of diabetes diagnosis in health insurance claims data in Taiwan. *J Formos Med Assoc*. 2005;104(3):157-163.
29. Young BA, Lin E, Von Korff M, et al. Diabetes complications severity index and risk of mortality, hospitalization, and healthcare utilization. *Am J Manag Care*. 2008;14(1):15-23.
30. Meduru P, Helmer D, Rajan M, Tripoli LC. Chronic illness with complexity: implications for performance measurement of optimal glycemic control. *J Gen Intern Med*. 2007;22(suppl 3):408-418.
31. Lee TT, Cheng SH, Chen CC, Lai MS. A pay-for-performance program for diabetes care in Taiwan: a preliminary assessment. *Am J Manag Care*. 2010;16(1):65-69.
32. Cheng SH, Lee TT, Chen CC. A longitudinal examination of a pay-for-performance program for diabetes care: evidence from a natural experiment. *Med Care*. 2012;50(2):109-116.
33. Huang P, Hsu YH, Kai-Yuan T, Hsueh YS. Can European external peer review techniques be introduced and adopted into Taiwan's hospital accreditation system? *Int J Qual Health Care*. 2000;12(3):251-254.
34. Diggle P, Heagerty P, Liang KY. *Analysis of Longitudinal*. New York, NY: Oxford; 2002.
35. Austin PC, Ghali WA, Tu JV. A comparison of several regression models for analysing cost of CABG surgery. *Stat Med*. 2003;22(17):2799-2815.
36. Adler AI, Stevens RJ, Manley SE, et al. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). *Kidney Int*. 2003;63(1):225-232.
37. Fox CS, Sullivan L, D'Agostino RB Sr, Wilson PW; Framingham Heart Study. The significant effect of diabetes duration on coronary heart disease mortality: the Framingham Heart Study. *Diabetes Care*. 2004;27(3):704-708.
38. Vink NM, Klunge OH, Stolk RP, Denig P. Comparison of various measures for assessing medication refill adherence using prescription data. *Pharmacoepidemiol Drug Saf*. 2009;18(2):159-165. ■

eAppendix A

Table 1-1. GEE Regression Analysis of Medication Adherence and Healthcare Outcomes Using Different Definitions of DM-Related Conditions

Variables	Sokol et al (2005) ¹²						Bethel et al (2007) ¹					
	Model 1			Model 2			Model 1			Model 2		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Hospitalization for DM or cardiovascular/cerebrovascular-related conditions												
Adherence (reference group: nonadherence [MPR <80%])	0.76	0.71	0.81	0.80	0.74	0.88	0.74	0.69	0.79	0.79	0.72	0.86
Duration of 5 years or more (reference group: less than 5 years)	1.28	1.22	1.36	1.41	1.27	1.56	1.30	1.23	1.37	1.43	1.29	1.58
Interaction between medication adherence and duration of DM	-	-	-	0.88	0.78	0.99	-	-	-	0.87	0.77	0.98
ED visits for DM or cardiovascular/cerebrovascular-related conditions												
Adherence (Reference group: nonadherence [MPR <80%])	0.80	0.73	0.88	0.87	0.77	0.98	0.76	0.70	0.83	0.84	0.75	0.95
Duration of 5 years or more (reference group: less than 5 years)	1.32	1.22	1.42	1.47	1.28	1.70	1.33	1.24	1.43	1.53	1.34	1.75
Interaction between medication adherence and duration of DM	-	-	-	0.86	0.73	1.01	-	-	-	0.82	0.70	0.96

CI indicates confidence interval; CIC index count, chronic illness with complexity index count; DCSI, diabetes complications severity index; DM, diabetes mellitus; ED, emergency department; GEE, generalized estimation equation; MPR, medication possession ratio; OR, odds ratio; P4P, pay-for-performance.

All models were controlled for sex, age groups, number of physician visits by tertiles, DCSI score, CIC index count, hospitalization in the previous year, intensity of the DM drug regimen, number of medications per prescription ≥ 3 , enrollment in the P4P program, accreditation level of the hospital most frequently visited for diabetes care, and speciality of the physician most frequently seen for diabetes care.

Table 1-2. GEE Regression Analysis of Medication Adherence and Healthcare Expenses Using Different Definitions of DM-Related Conditions

Variables	Sokol et al (2005) ¹²						Bethel et al (2007) ¹					
	Model 1			Model 2			Model 1			Model 2		
	β	SE	<i>P</i>	β	SE	<i>P</i>	β	SE	<i>P</i>	β	SE	<i>P</i>
Expenses for hospitalizations or ED visits for DM or cardiovascular/cerebrovascular-related conditions												
Adherence (reference group: nonadherence [MPR<80%])	-0.48	0.08	<.001	-0.37	0.10	<.001	-0.57	0.08	<.001	-0.42	0.10	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.55	0.07	<.001	0.73	0.12	<.001	0.58	0.07	<.001	0.82	0.12	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.25	0.15	.094	-	-	-	-0.34	0.14	.018

CIC index count indicates chronic illness with complexity index count; DM, diabetes mellitus; DCSI score, diabetes complications severity index score; ED, emergency department; GEE, generalized estimation equation; MPR, medication possession ratio; P4P program, pay-for-performance program; SE, standard error.

All models were controlled for sex, age groups, number of physician visits by tertiles, DCSI score, CIC index count, hospitalization in the previous year, intensity of the DM drug regimen, number of medications per prescription ≥ 3 , enrollment in the P4P program, accreditation level of the hospital most frequently visited for diabetes care, and specialty of the physician most frequently seen for diabetes care.

eAppendix B

Table 2-1. GEE Regression Analysis of Medication Adherence and Healthcare Outcomes Using Different Cut-Off Points for MPR

	Model 1			Model 2		
	OR	95% CI		OR	95% CI	
Hospitalization for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <70%])	0.77	0.72	0.83	0.87	0.79	0.96
Duration of 5 years or more (reference group: less than 5 years)	1.26	1.20	1.33	1.57	1.39	1.77
Interaction between medication adherence and duration of DM	-	-	-	0.76	0.67	0.87
Hospitalization for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <90%])	0.72	0.68	0.76	0.75	0.69	0.81
Duration of 5 years or more (reference group: less than 5 years)	1.29	1.22	1.36	1.34	1.23	1.46
Interaction between medication adherence and duration of DM	-	-	-	0.93	0.84	1.04
ED visits for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <70%])	0.80	0.73	0.87	0.85	0.76	0.95
Duration of 5 years or more (reference group: less than 5 years)	1.25	1.17	1.33	1.40	1.22	1.61
Interaction between medication adherence and duration of DM	-	-	-	0.86	0.74	1.01
ED visits for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <90%])	0.80	0.74	0.85	0.81	0.74	0.90
Duration of 5 years or more (reference group: less than 5 years)	1.26	1.18	1.34	1.29	1.17	1.42
Interaction between medication adherence and duration of DM	-	-	-	0.96	0.84	1.09

CI indicates confidence interval; CIC index count, chronic illness with complexity index count; DCSI, diabetes complications severity index; DM, diabetes mellitus; ED, emergency department; GEE, generalized estimation equation; MPR, medication possession ratio; OR, odds ratio; P4P, pay-for-performance.

All models were controlled for sex, age groups, number of physician visits by tertiles, DCSI score, CIC index count, hospitalization in the previous year, intensity of the DM drug regimen, number of medications per prescription ≥ 3 , enrollment in the P4P program, accreditation level of the hospital most frequently visited for diabetes care, and specialty of the physician most frequently seen for diabetes care.

Table 2-2. GEE Regression Analysis of Medication Adherence and Healthcare Expenses Using Different Cut-Off Points for MPR

Variables	Model 1			Model 2		
	β	SE	<i>P</i>	β	SE	<i>P</i>
Drug expenses for oral antihyperglycemic medications						
Adherence (reference group: non-adherence [MPR <70%])	0.65	0.01	<.001	0.66	0.01	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.12	0.00	<.001	0.15	0.01	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.04	0.01	.002
Drug expenses for oral antihyperglycemic medications						
Adherence (reference group: nonadherence [MPR <90%])	0.39	0.01	<.001	0.43	0.01	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.13	0.00	<.001	0.18	0.01	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.09	0.01	<.001
Expenses for hospitalizations or ED visits for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <70%])	-0.36	0.09	<.001	-0.18	0.11	.117
Duration of 5 years or more (reference group: less than 5 years)	0.53	0.07	<.001	0.86	0.15	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.42	0.17	.014
Expenses for hospitalizations or ED visits for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <90%])	-0.49	0.07	<.001	-0.37	0.10	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.55	0.07	<.001	0.70	0.10	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.25	0.13	.062
Total healthcare expenses for any condition						
Adherence (reference group: nonadherence [MPR <70%])	0.14	0.01	<.001	0.22	0.02	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.13	0.01	<.001	0.29	0.02	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.20	0.02	<.001
Total healthcare expenses for any condition						
Adherence (reference group: nonadherence [MPR <90%])	0.07	0.01	<.001	0.13	0.01	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.13	0.01	<.001	0.21	0.01	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.13	0.02	<.001

CIC index count indicates chronic illness with complexity index count; DCSI, diabetes complications severity index; DM, diabetes mellitus; ED, emergency department; GEE, generalized estimation equation; MPR, medication possession ratio; P4P, pay-for-performance; SE, standard error.

All models were controlled for sex, age group, number of physician visits by tertiles, DCSI score, CIC index count, hospitalization in the previous year, intensity of the DM drug regimen, number of medications per prescription ≥ 3 , enrollment in the P4P program, accreditation level of the hospital most frequently visited for diabetes care, and specialty of the physician most frequently seen for diabetes care.

eAppendix C

Table 3-1. Patient Characteristics in the First Year Following Diabetes Diagnosis in Pre- and Post PSM Samples

Variables	Pre-PSM sample					Post-PSM sample				
	Nonadherent group		Adherent group		<i>P</i>	Nonadherent group		Adherent group		<i>P</i>
	N	%	N	%		N	%	N	%	
Total	5201		6379			3864		3864		
Sex					.006					.495
Male	2832	54.45	3309	51.87		1952	50.52	1982	51.29	
Female	2367	45.51	3066	48.06		1912	49.48	1882	48.71	
Missing	2	0.04	4	0.06		-	-	-	-	
Age groups, y					<.001					.935
18-44	990	19.03	1021	16.01		651	16.85	639	16.54	
45-64	3166	60.87	3869	60.65		2378	61.54	2388	61.80	
65+	1045	20.09	1489	23.34		835	21.61	837	21.66	
Number of physician visits by tertiles					<.001					.489
Low	1865	35.86	762	11.95		695	17.99	729	18.87	
Medium	1716	32.99	2683	42.06		1578	40.84	1535	39.73	
High	1620	31.15	2934	45.99		1591	41.17	1600	41.41	
Hospitalizations in the previous year	548	10.54	773	12.12	<.001	476	12.32	401	10.38	.484
DCSI score					<.001					.925
Score 0	3461	66.54	3606	56.53		2398	62.06	2392	61.90	
Score 1	1097	21.09	1625	25.47		908	23.50	902	23.34	
Score 2+	643	12.36	1148	18.00		558	14.44	570	14.75	
CIC index count					.282					.514
0	1927	37.05	2434	38.16		1314	34.01	1327	34.34	
1	2005	38.55	2462	38.60		1512	39.13	1543	39.93	
2+	1269	24.40	1483	23.25		1038	26.86	994	25.72	
Multiple oral antihyperglycemic medications	2445	47.01	3617	56.70	<.001	1927	49.87	1938	50.16	.802
Number of medications per prescription ≥ 3	3145	60.47	4017	62.97	.006	2416	62.53	2447	63.33	.465
Enrolled in P4P program	166	3.19	531	8.32	<.001	149	3.86	150	3.88	.953
Accreditation level of hospitals					<.001					.423
Medical center	597	11.48	1579	24.75		562	14.54	610	15.79	
Regional hospitals	1043	20.05	1804	28.28		869	22.49	832	21.53	
District hospitals	1086	20.88	1155	18.11		792	20.50	786	20.34	
Clinics	2475	47.59	1841	28.86		1641	42.47	1636	42.34	
Metabolism endocrinologist	83	1.60	177	2.77	<.001	71	1.84	69	1.79	.865

CIC index count indicates chronic illness with complexity index count; DCSI, diabetes complication severity index; P4P, pay-for-performance; PSM, propensity score matching; SD, standard deviation.

Table 3-2. GEE Regression Analysis of Medication Adherence and Healthcare Outcomes, Using PSM Approach

Variables	Model 1			Model 2		
	OR	95% CI		OR	95% CI	
Hospitalization for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <80%])	0.77	0.72	0.84	0.85	0.77	0.95
Duration of 5 years or more (reference group: less than 5 years)	1.23	1.15	1.31	1.43	1.27	1.61
Interaction between medication adherence and duration of DM	-	-	-	0.81	0.70	0.93
ED visits for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <80%])	0.80	0.73	0.88	0.83	0.73	0.93
Duration of 5 years or more (reference group: less than 5 years)	1.26	1.16	1.36	1.32	1.14	1.51
Interaction of medication adherence and duration of DM	-	-	-	0.94	0.79	1.11

CI indicates confidence interval; CIC index count, chronic illness with complexity index count; DCSI, diabetes complications severity index; DM, diabetes mellitus; ED, emergency department; GEE, generalized estimation equation; MPR, medication possession ratio; OR, odds ratio; P4P program, pay-for-performance program; PSM, propensity score matching;

All models were controlled for sex, age groups, number of physician visits by tertiles, DCSI score, CIC index count, hospitalization in the previous year, intensity of the DM drug regimen, number of medications per prescription ≥ 3 , enrollment in the P4P program, accreditation level of the hospital most frequently visited for diabetes care, and specialty of the physician most frequently seen for diabetes care.

Supplementary Table 3-3. GEE Regression Analysis of Medication Adherence and Healthcare Expenses, Using PSM Approach

Variables	Model 1			Model 2		
	β	SE	<i>P</i>	β	SE	<i>P</i>
Drug expenses for oral antihyperglycemic medications						
Adherence (reference group: nonadherence [MPR <80%])	0.11	0.01	<.001	0.18	0.02	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.12	0.01	<.001	0.24	0.02	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.16	0.03	<.001
Expenses for hospitalizations or ED visits for DM or cardiovascular/cerebrovascular-related conditions						
Adherence (reference group: nonadherence [MPR <80%])	0.51	0.01	<.001	0.54	0.01	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.13	0.01	<.001	0.17	0.01	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.06	0.01	<.001
Total healthcare expenses for any condition						
Adherence (reference group: nonadherence [MPR <80%])	-0.62	0.08	<.001	-0.45	0.11	<.001
Duration of 5 years or more (reference group: less than 5 years)	0.50	0.08	<.001	0.78	0.13	<.001
Interaction between medication adherence and duration of DM	-	-	-	-0.40	0.16	.011

CIC index count indicates chronic illness with complexity index count; DCSI, diabetes complications severity index; DM, diabetes mellitus; ED, emergency department; GEE, generalized estimation equation; MPR, medication possession ratio; P4P, pay-for-performance; PSM, propensity score matching; SE, standard error.

All models were controlled for sex, age group, number of physician visits by tertiles, DCSI score, CIC index count, hospitalization in the previous year, intensity of the DM drug regimen, number of medications per prescription ≥ 3 , enrollment in the P4P program, accreditation level of the hospital most frequently visited for diabetes care, and specialty of the physician most frequently seen for diabetes care.