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A study on the impact of poor medication adherence on health status and medical expense for diabetes mellitus patients in Taiwan

A longitudinal panel data analysis

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Abstract

Medication adherence plays an important role in disease management, especially for diabetes. The aim of this study was to examine the impacts of demographic characteristics on medication nonadherence and the impacts of nonadherence on both health status and medical expenses for diabetic patients in Taiwan.

A total of 1 million diabetes mellitus patients were randomly selected from the National Health Insurance Research Database between January 1, 2000 and December 31, 2004. All records with missing values and those for participants under 18 years of age were then deleted. Because many patients had multiple clinical visit records, all records within the same calendar year were summarized into 1 single record for each person. This pre-processing resulted in 14,602 total patients with a combined 73,010 records over the course of 5 years. Generalized estimating equation models were then constructed to investigate the effects of demographic characteristics on medication nonadherence and the effects of nonadherence on patient health status and medical expenses. The demographic characteristics examined for each patient include gender, age, residential area, and socioeconomic status.

Our analysis of how demographic variables impacted nonadherence revealed that elderly patients exhibited better overall medication adherence, but that male patients exhibited poorer medication adherence than female patients. Next, our analysis of how nonadherence impacted health status revealed that patients who exhibited medication nonadherence had poorer health status than patients with proper medication adherence. Finally, our analysis of how nonadherence impacted medical expenses revealed that patients who exhibited medication nonadherence incurred more medical expenses than those who exhibited proper medication adherence.

This study's empirical results corroborate the general relationships expressed in the current literature regarding medication nonadherence. However, this study's results were statistically more reliable and revealed the precise impact on health status in terms of the Charlson comorbidity index and increased annual medical expenses. This indicates the need to improve patient attitudes toward medication adherence, which can have substantial effects both medically and economically.

Abbreviations: CCI = Charlson comorbidity index, GEE = generalized estimating equation.

Keywords: Charlson comorbidity index, diabetes mellitus, generalized estimating equation model, health care costs, medication adherence

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The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

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1. Introduction

Diabetes mellitus is an incurable disease that is increasing in both incidence and prevalence.[1] In 2017, the International Diabetes Federation Diabetes Atlas showed that an estimated 451 million people were suffering from the disease worldwide.[2] Diabetes mellitus can result in various macro-vascular and micro-vascular complications that substantially impact both patient health and the medical system in general. However, adequate blood sugar control is known to reduce the risk of cardiovascular and microvascular complications for diabetes patients.[3] In this regard, adequate treatment is not only important for individual health status among diabetic mellitus patients but also has substantial implications for resource utilization throughout the medical system.

Reports indicated that patient noncompliance for diabetes treatment is around 50% in developed countries and maybe even higher in developing countries.[4] Among the key treatments for diabetes mellitus, medical compliance is a main area of concern; indeed, it has been discussed in the literature from many different perspectives.[5]

This study explored the impacts of demographic characteristics on patient medication nonadherence, medication nonadherence on health status, and medication nonadherence on different medical expenses. In this regard, previous studies have produced unconvincing evidence due to several issues, such as the difficulty of data collection, insufficient sample size, and poor sample representativeness. As such, this study examined daily medical visit data from Taiwan's National Health Insurance Research Database (NHIRD) to explore the impact of the abovementioned relationships.

2. Methods

2.1. Ethical statement

This study was approved by the Institutional Review Board of the Buddhist Taichung Tzu Chi General Hospital, Taiwan (REC103-43). However, written consent was not obtained from each patient because all study data consisted of secondary files. In this regard, all identification numbers and personal information were deleted before the data were released from the NHIRD.

2.2. Dataset

The Taiwan National Health Insurance (NHI) program is a mandatory government-run enrollment service that characterizes the Taiwanese universal single-payer health insurance system. It was initiated in 1995 and contracts with over 97% of the medical facilities in Taiwan to provide health care services. Nearly 99% of the 23 million residents of Taiwan receive medical service in contracted facilities through the NHI program.[6] Further, patients who receive NHI medical services can obtain medications and pharmacy services at any NHI-contracted pharmacies. All data related to these medical and pharmacy services are then collected and recorded in the NHIRD by the National Health Research Institutes to provide a general record of medical care.

The NHIRD contains inpatient, outpatient, prescription information, and disease diagnosis files that are coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Naturally, this has been a very important data source for research in medicine and health-related fields. This study extracted all daily medical visit data for diabetic mellitus patients between January 1, 2000 and December 31, 2004.

2.3. Design and participants

Inclusion criteria for patients were as follows: 18 years of age or older, diagnosed with diabetes mellitus (ICD-9-CM Codes 250.xx), complications with diabetes mellitus (ICD-9-CM Codes 271.4, 357.2, 362.01–362.02, 366.41, 648.00–648.05, 750.0–750.1, 791.5, V18.0, V77.1), and receiving insulin, biguanides, sulfonamides, urea derivatives, a-glucosidase inhibitors, thiazolidinediones, dipeptidyl peptidase 4, or a combination of oral antihyperglycemic agents. Patients who had diabetes but who were not taking anti-hyperglycemic agents were excluded from the study. For patients who made multiple physician visits during the study period, we combined their information in accordance with the date of the relevant fee, application type, hospital identification code, and case sequence number. This was done to combine all records for each calendar year into 1 single annual record for each patient.

The final derived data files were obtained by merging different files, such as those for inpatient expenditures based on admissions files, ambulatory care expenditures based on visit files, details of inpatient order files, details of ambulatory care order files, registry for beneficiary files, registry for contracted medical facilities files, and registry for drug prescriptions files. The overall sample thereby spanned a 5-year period and included patients from a variety of residential areas. After deleting missing data and summarizing all records for each calendar year into 1 annual record for each patient, this resulted in 14,602 total patients with diabetes mellitus who were taking anti-hyperglycemic medications.

We also used the database to collect and/or calculate demographic and other information, including gender, age, socio-economic status, living area, level of visited hospitals, and total annual medical visit expenses for each patient. Gender was noted as a binary (ie, 1 for male, 0 otherwise), while age was calculated for each patient based on the number of months between their respective birthday and the day of the medical visit. Socio-economic status was determined based on the amount of insurance expenses paid yearly; if expenses were greater than or equal to NT$ 120,000, then the patient was categorized as having high socio-economic status. However, such expenses amounting to less than NT$ 120,000 were used to indicate low socio-economic status. Living area was determined based on the 4 total residential areas of Taiwan: the north, center, south, and east. Next, the levels of the visited hospitals were determined based on 4 classes: Medical Centers, Regional Hospitals, District Hospitals, and General Practice Clinics. The numerical values of all variables used in this study's research model were calculated based on raw data to avoid possible biases incurred during questionnaire collection (eg, answers from memory and those disguised through social norms).

2.4. Medication adherence and follow-up

The World Health Organization defines medication adherence as the "the degree to which the person's behavior corresponds with the agreed recommendations from a health care provider."[7] This most often refers to medication or drug compliance but can also apply to medical device usage, self-care, self-directed exercises, and/or therapy sessions. The literature is characterized by 2 approaches for measuring medication adherence, including the medication possession ratio (MPR) and proportions of days covered (PDC). MPR measures the percentage of time a given patient has access to medication; it is the sum of the days' supply for all fillings of a given drug during a particular time period divided by the number of days in that time period. PDC is the proportion of days in the measurement period "covered" by prescription claims for the same medication or another in its therapeutic category. The MPR is a popular measurement for adherence within the context of the health care industry.[8] However, some researchers favor the PDC because it eliminates the problem of overlapping prescriptions during the specifically investigated period.

This study examined medication adherence with a focus on medication compliance, which is represented as the MPR. First, MPR is more broadly used than PDC in studies on medication adherence. Second, chronically ill patients may avoid medical facilities if their illnesses are not severe and/or if they have residual drugs; this is especially true among the elderly. As such, we preferred MPR over PDC as a proxy for medication adherence in the stipulated situations. In this study, MPR was calculated using the following formula: MPR = total number of days' supply obtained between the first and last fills (excluding the last fill) divided by the number of days between the first and last fills.[9] High medication compliance was defined as patients with MPRs greater than or equal to 80%, while patients with MPRs less than 80% were defined as having low medication compliance. In order to more accurately describe compliance willingness, we did not count days when patients were staying in hospitals.

2.5. Main outcome measurements and covariate assessment

2.5.1. Health status and the Charlson comorbidity index (CCI). Diabetes mellitus is a lifelong disease that may result in complications leading to substantial damage to the patient's quality of life.[10] A given diabetic mellitus patient usually experiences 3 to 4 complications simultaneously.[11] As such, a common way to measure diabetic mellitus severity is through comorbidities listed in the literature. Comorbidity refers to the presence of 1 or more additional diseases/disorders that co-occur with a primary disease/disorder.

Charlson, Pompei, Ales, and MacKenzie[12] developed the CCI to measure the severity of health status for patients with multiple diseases; here, higher indexes indicate lower survival probability.[13] Different versions of the CCI have been developed to adapt clinical comorbidity indices to specific diseases.[14–16] One of this study's aims was to elaborate the effects of medicine compliance on health among diabetes patients. In this regard, it is imperative to find a dependent variable that can be measured to reflect the health status of diabetes mellitus patients. However, there is no such commonly used measurement in the current literature. Because diabetes mellitus is a systemic disease that may cause macro- and micro-vascular disorders in multiple organs (eg, nephropathy, retinopathy, and neuropathy, which are major diabetes complications), it is also associated with other diseases or syndromes, including stroke, heart disease, and electrolyte disorders resulting from hyperosmolar hyperglycemic status. Thus, diabetes mellitus complications and comorbidities should be included when measuring the health status of a given diabetes mellitus patient. As the CCI produces a weighted sum of some especially important complications and comorbidities, it has been used to predict a variety of outcomes, including the mortality of type 2 diabetes mellitus nephropathy[17] and subsequent hospitalizations among type 2 diabetes mellitus patients.[18] Further, a study in northern Denmark revealed a positive predictive value of 82.0% (95% confidence interval; 68.6%, 91.4%) for CCI when used among diabetes patients with diabetic complications.[19] Taken together, the evidence shows that the CCI is an appropriate proxy for measuring health status among diabetes mellitus patients in regard to the complications of comorbidities.

This study used Deyo version of the CCI due to the availability of relevant variables in the database.[14] The examined comorbidities included myocardial infarction (ICM-9-CM Code 410–410.9, 412), congestive heart failure (ICM-9-CM Code 428–428.9), peripheral vascular disease (ICM-9-CM Code 443.9, 441, 441.9, 785.4, V43.4), cerebrovascular disease (ICM-9-CM Code 430–438), dementia (ICM-9-CM Code 290–290.9), chronic pulmonary disease (ICM-9-CM Code 490–496, 500–505, 506.4), rheumatologic disease (ICM-9-CM Code 710.0, 710.1, 710.4, 714.0–714.2, 714.81, 725), peptic ulcer disease (ICM-9-CM Code 531–534.9), mild liver disease (ICM-9-CM Code 571.2, 571.5, 571.6, 571.4–571.49), diabetes (ICM-9-CM Code 250–250.3, 250.7), diabetes with chronic complications (ICM-9-CM Code 250.4–250.6), hemiplegia or paraplegia (ICM-9-CM Code 344.1, 342–342.9), renal disease (ICM-9-CM Code 582–582.9, 583–583.7, 585, 586, 588–588.9), any malignancy (including leukemia and lymphoma) (ICM-9-CM Code 140–172.9, 174–195.8, 200–208.9), moderate or severe liver disease (ICM-9-CM Code 572.2–572.8, 456.0–456.21), metastatic solid tumor (ICM-9-CM Code 196–199.1), and acquired immunodeficiency disease (AIDS) (ICM-9-CM Code 042–044.9).[14]

2.5.2. Medical expenses. Medical expenses include those incurred from clinics, emergency rooms, ordinary wards, and intensive care units. These are correlated with patient medication adherence. For example, patients exhibiting proper medication adherence paid higher fees at clinics but less for hospitalizations. On the other hand, patients exhibiting poor medication adherence spent more money for services in emergency rooms, ordinary wards, and intensive care units due to comorbidities and developed complications. This study collected medical expense data per person per year, including clinical expenditures, emergency treatment expenses, hospitalization costs, and expenses incurred at intensive care units. This was done to explore how patients were affected by medication nonadherence. Moreover, in this study, we considered the severity of illness for diabetic patients and calculated their expenditures for diabetes in emergency rooms, ordinary wards, and intensive care units. We then analyzed the relationships among these costs and the degree of morbidity among diabetic patients.

2.5.3. Statistical analyses. The SAS 9.4 software was used for all data analyses. A total of 3 models were constructed to investigate the relationships among variables. In this context, the generalized estimating equations (GEE) method is commonly applied to evaluate the associations among repeated observations in panel data. The model is used to replace basic regression because repeated measurements are correlated, thereby violating the assumptions of independence found in traditional regression models.[20] Based on the characteristics of the dataset, GEE models were thus constructed to explore the relationships among the variables examined in this study.

3. Results

In addition to descriptions of patient characteristics, the impacts of these demographic variables on nonadherence, and the impacts of nonadherence on both health status and medical expenses are outlined in the following passages.

3.1. Patient characteristics

A total of 14,602 diabetes mellitus patients were derived from the dataset. Patient records were then combined to result in annual records for each patient from 2000 to 2004 (5 years). The basic statistics are listed in Table 1. As the table shows, 48.79% of patients were male and 51.21% were female, while the average age was 61.74 years with a standard deviation equal to 11.13 years. For residential area, 43.14%, 17.76%, 36.02%, and 3.07% lived in the north, center, south, and east, respectively. Next, 19.2% were of high socio-economic status, while 80.8% were of low socio-economic status. Finally, 36.1%, 20.35%, 22.67%, and 20.87% visited medical centers, regional hospitals, district hospitals, and general practice clinics, respectively.

Medication adherence was defined as high ($y=1$) when MPR was greater than or equal to 80% and as low ($y=0$) when MPR was less than 80%; this method followed the threshold values established by McGovern, Tippu, Hinton, Munro, Whyte, and de Lusignan.[21] The average MPR was 0.637 with a standard deviation equal to 0.274. The proportions for high and low medication adherence were 75.27% and 24.73%, respectively.

Table 1

Baseline characteristics.

Variables	No. of patients	Percentage
Male	7125	48.79%
Female	7477	51.21%
Age, mean (SD), yr		61.74 (11.13)
Residential area		
North	6300	43.14%
Center	2593	17.76%
South	5260	36.02%
East	449	3.07%
Socio-economic status		
High	2804	19.20%
Low	11,798	80.80%
Hospital grade		
Medical center	5272	36.10%
Regional hospital	2972	20.35%
District hospital	3311	22.67%
Local clinics	3047	20.87%
Medication adherence		
High MPR	10,991	75.27%
Low MPR	3611	24.73%

In the analysis, the population of for residential area in the North Taiwan is more than South, Central, and East Taiwan, similar with the distribution of population of Taiwan in the study period. Participants of low socio-economic status is more than that of high socio-economic status. Most participants have high medication adherence.

MPR = medication possession ratio, SD = standard deviation.

3.2. Empirical results for impacts of patients characteristics on medication adherence

Each patient had 1 record for each year (5 years total). A GEE model was then constructed with medication adherence as the dependent variable, while demographic and medical-behavior variables were set as independent variables. Further, medical central and north Taiwan served as references for the medical institution level and residential area variables. The empirical results are listed in Table 2.

As Table 2 shows, medication adherence was lower among male patients and was positively impacted by age. Patients who visited different levels of hospitals revealed different levels of medication adherence. Compared with patients living in north Taiwan, those living in south and east Taiwan exhibited lower medication adherence. And there is no significant difference between those living in north and central Taiwan.

3.3. Empirical results for impacts of medication nonadherence on health status

The annual means and standard deviations of CCI for all patients are listed in Table 3. Here, an increasing trend was evident. Further, results of the ANOVA on CCI among these years were statistically significant; a post-hoc comparison also showed that differences between any consecutive years were statistically significant. The average CCI for all patients in the sample is 3.07 with a standard deviation equal to 2.29.

Table 2

The GEE results for medication adherence on demographic variables.

Parameter	Beta	Standard error	Confidence interval		Pr > |Z|
Intercept	0.1183‡	0.015	0.0889	0.1477	<0.0001
Gender	−0.0108†	0.0052	−0.0211	−0.0005	0.0395
Age	0.0038‡	0.0002	0.0033	0.0043	<0.0001
Socio-economic status	0.0041	0.0069	−0.0094	0.0176	0.551
Hospital grade					
Regional	0.0155‡	0.0058	0.0042	0.0268	0.0071
District	0.0251‡	0.0055	0.0143	0.0359	<0.0001
Local clinics	0.0199‡	0.0055	0.009	0.0308	0.0003
Residential area					
Center	0.0001	0.0074	−0.0145	0.0147	0.9853
South	−0.0557‡	0.0058	−0.0671	−0.0444	<0.0001
East	−0.0626‡	0.0149	−0.0918	−0.0334	<0.0001

In generalized estimating equations (GEE) model, gender, age, hospital grade, and residential area have impact on medication adherence.

† *P*-value < .05.

‡ *P*-value < .01.

Table 3

The average CCI for all the diabetic mellitus patients from 2000 to 2004.

Year	Mean	Standard deviation
2000	1.706	1.470
2001	2.396	2.013
2002	3.047	2.510
2003	3.704	3.020
2004	4.483	3.679

There is growing trend of the severity of the health status of patients.
CCI = the Charlson comorbidity index.

Table 5

Different medical expenses for each year from 2000–2004.

Year	OPD	ADM	ER	ICU
2004	57471.64	23910.95	1513.81	1652.73
2003	48876.45	16333.06	1233.62	1030.11
2002	43455.05	14353.17	1052.24	709.96
2001	36727.96	11494.83	796.31	461.54
2000	32899.04	10117.77	768.91	366.99

ADM = admission to ordinary ward; service fee in Taiwan dollars, ER = emergency room, ICU = admission to intensive care unit, OPD = outpatient department.

A GEE model was then constructed with CCI as the dependent variable, while demographic and medical-behavior variables were set as independent variables (Table 4). Except for socio-economic status, all independent variables statistically and significantly impacted CCI. Notably, MPR had a negative impact on CCI.

3.4. Empirical results for impacts of medication nonadherence on medical expenses

Data on clinical expenditures, hospitalization costs, emergency treatment expenses, and expenses incurred in intensive care units were collected for each patient. Table 5 shows that each item increased over the 5-year period of study. Notably, hospitalization costs, emergency treatment expenses, and expenses incurred in intensive care units doubled or more during that time. In other words, medical expenses increased annually in every category of medical expenses for each patient.

GEE models were also constructed for each expense item to determine how the demographic and medical-behavior variables affected expenses (Table 6). As shown, MPR effects differed based on the type of medical cost. That is, MPR had a positive impact on clinical expenses but a negative impact on admissions, emergency room, and intensive care unit expenses.

4. Discussion

As shown in Table 1, 36% of diabetes patients visited medical centers for treatment. The proportions for the other 3 types of medical institutions were 20.35%, 22.67%, and 20.87% for regional hospitals, district hospitals, and local clinics respectively, thus indicating the availability and popularity of particular medical resources in Taiwan. As shown in Table 2, medication adherence was significantly higher among patients who visited regional hospitals, district hospitals, and clinics when compared to patients who visited medical centers. Further study is needed to determine the reasons for the low medication adherence found among patients who visit Taiwanese medical centers.

This study used the CCI index as a proxy for health status among diabetic mellitus patients; here, higher index values indicated worse health status. As shown in Table 3, the index increased at a rate of 0.8 each year for all patients. As such, it is a sufficient indicator of how effectively the medical system controls diabetic mellitus. When compared to the CCI index values found among patients who visited medical centers, those found among patients who visited regional hospitals, district hospitals, and general practice clinics were 0.237, 0.471, and 0.03, respectively. This can be further studied to investigate what causes these differences.

As shown in Table 4, patients with high medication adherence had lower CCI index values than those with low medication adherence. The empirical results of the GEE model shown in Table 6 also indicate that male patients generated more medical expenses in admissions and at intensive care units than female patients. Further, age was found to have a significantly positive influence on all medical expenses except those incurred at emergency rooms. Next, patients of high socio-economic status spent less on all medical expenses except those incurred at clinics.

Table 4

GEE results for CCI on demographic variables and medical behavior.

Independent	Estimate	SE	95% CI		Z	Pr > |Z|
Intercept	−1.765‡	0.110	−1.981	−1.549	−16.000	<0.0001
Gender	0.063*	0.037	−0.011	0.136	1.680	0.093
Age	0.069‡	0.002	0.066	0.072	40.120	<0.0001
Socio-economic status	−0.018	0.046	−0.108	0.073	−0.380	0.702
Hospital Grade						
Regional	0.237‡	0.021	0.196	0.277	11.540	<0.0001
District	0.471‡	0.022	0.429	0.513	21.870	<0.0001
Local Clinics	0.300‡	0.022	0.256	0.343	13.410	<0.0001
Residential Area						
Center	0.057	0.051	−0.043	0.157	1.120	0.261
South	0.171‡	0.041	0.090	0.251	4.130	<0.0001
East	0.049	0.110	−0.167	0.265	0.440	0.656
MPR	−0.059‡	0.012	−0.083	−0.036	−4.920	<0.0001

The null hypothesis is rejected if Pr > |Z| is lower than the conventional threshold of 0.05.
* P-value < .1.
‡ P-value < .01.
CI = confidence interval, GEE = generalized estimating equations, MPR = medication possession ratio, SE = standard error.

Table 6

The GEE results for different medical expenses on demographic variables and medical behavior.

Variables	OPD Model 1	Hospitalization Model 2	ER Model 3	ICU Model 4
Intercept	13422.510‡	−16791.900‡	−578.854‡	−1548.430‡
Gender	−448.985	1791.798‡	50.2031	149.809*
Age	158.268‡	72.080‡	2.647	7.958†
Socio-economic status	−1205.35	−2404.010‡	−259.876‡	−196.064‡
Hospital grade				
Regional	1436.799‡	1986.482‡	−79.2094†	−125.327*
District	4065.938‡	10910.560‡	365.401‡	656.972‡
Clinical	8081.516‡	14282.300‡	761.898‡	629.981‡
Residential area				
Center	−1332.32	31.2087	−164.909‡	72.7949
South	−4081.680‡	298.714	−177.630‡	9.5612
East	−8679.030‡	2671.900*	−31.7646	40.7758
CCI	6464.178‡	4911.163‡	310.353‡	393.027‡
MPR	1388.160‡	−5089.700‡	−275.470‡	−326.857‡

* $P<.1$.
† $P<.05$.
‡ $P<.01$.
ADM = admission to ordinary ward, CCI = Charlson comorbidity index, ER = emergency room, GEE = generalized estimating equations, ICU = admission to intensive care unit, MPR = medication possession ratio, OPD = outpatient department.

Finally, high medical compliance was associated with increased clinical expenditures but lower emergency room expenditures in both ordinary wards and intensive care units. In other words, patients exhibiting high medical compliance made more frequent medical visits than those exhibiting low medical compliance; it is thus reasonable for these patients to have greater clinical expenditures. However, patients exhibiting high medication adherence possibly had better overall health status, which may be associated with lower amounts of hospitalization, emergency treatment, and intensive care unit expenses. Numerically, the results showed that the total expenses for patients exhibiting high medication adherence were NT 4304 dollars less than those of patients exhibiting low medication adherence (1388.16–5089.7–275.47–326.857 = 4304).

5. Conclusions

This study explored the relationships among patient demographics, medical behaviors, CCI index values, and medical expenses through an existing database. Because of the characteristics of the examined dataset, the utilization of a longitudinal approach, the amount of examined data, appropriate objectivity, sufficient representativeness, the use of a panel data analysis tool, and the employment of GEE models, this study revealed the impact of demographics and medical behaviors on patient outcomes in a more rigorous way than previous studies. As such, important policy implications can thereby be derived.

This study's results clearly demonstrate that several important factors affect medicine nonadherence. First, medication adherence was higher among female patients and the elderly, thus implying that medication adherence should specifically be further promoted among male and younger patients. Second, patients of regional hospitals, district hospitals, and general practice clinics exhibited higher medication adherence than those of medical centers, thus suggesting that medical centers should take immediate action to facilitate patient medical compliance. Third, based on the CCI results, diabetes patients who exhibited medication adherence had better control than those who exhibited medication nonadherence. Finally, patients who exhibited high medication adherence spent less each year on total medical expenses. Based on these last 2 results, diabetic patients with proper medicine compliance can maintain CCI while saving money on clinical costs.

This study had 4 main limitations. First, the NHIRD did not include several potential confounding factors, including emotional support, lifestyle, family support and conflict, and living environment. Second, MPR is measured by applying prescription refill patterns, which could overestimate real drug consumption rates.[22] Third, this study did not record other medications that patients were taking at the same time, nor did it consider clinical illnesses that may have impeded medication adherence. Finally, this study was only an investigation of the relationships among the same variables in 1 country; its approach should be extended to investigate these relationships in other countries through similar respective databases.

Author contributions

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