

Effect of Pharmacist-Led Interventions on Medication Adherence and Glycemic Control in Type 2 Diabetic Patients: A Study from the Chinese Population

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Purpose: Medication adherence plays an important role in glycemic control in type 2 diabetes mellitus (T2DM) self-management. To analyze the factors influencing medication adherence in T2DM patients and the effect of pharmacist-led interventions, we conducted a study in Beijing, China.

Patients and Methods: T2DM patients with hypoglycemic drugs for at least 6 months were enrolled. A pharmacist-led survey was conducted followed by individualized interventions for those non-adherent patients monthly within 3 months. FPG, HbA1c, and 2hPG were measured as the comprehensive glycemic control. Medication adherence was determined according to the patient's self-reported compliance with prescribed medication during the last 3 months.

Results: A total of 763 T2DM patients were included. The average age was 63.26±11.89 years, with 363 males. After pharmacist intervention, the patients with good adherence increased from 34.21% to 39.06%, while poor adherence decreased from 32.5% to 24.5% ($p < 0.001$). The average adherence score was a significant increase ($p < 0.001$) from 27.846±4.185 to 29.831±7.065. Furthermore, our study demonstrated that pharmacist-led interventions significantly increased glycemic control (FPG from 42.33% to 53.60%, $p < 0.001$; 2hPG from 41.68% to 48.75%, $p = 0.005$; HbA1c from 24.12% to 29.23%, $p = 0.024$). The results found that body mass index (OR 0.643, 95% CI 0.437–0.945), use of medications empirically (occasionally (OR=3.066, 95% CI 2.069–4.543); often (OR=2.984, 95% CI 1.107–8.044)), following the doctor's advice to visit (OR 2.129, 95% CI 1.079–4.202) and lifestyle compliance (OR 2.835, 95% CI 1.094–7.346) were the independent risk factors of non-adherence ($p < 0.05$), the area under the ROC curve was 0.716.

Conclusion: Self-reported medication adherence and glycemic control in T2DM patients were poor which can be improved by pharmacist-led interventions. Interventions should focus on empirical medication behavior, non-adherence to lifestyle, and failure to follow the doctor's advice. The recall bias with self-reported results needs further objective data to verify.

Keywords: T2DM, medication adherence, glycemic control, current status, risk factor, pharmacist-led interventions

Introduction

Over the past few decades, the incidence of diabetes worldwide has been increasing rapidly year by year, causing a huge burden on people's lives and the economy.¹ Type 2 diabetes mellitus (T2DM) is the most prevalent type of diabetes, accounting for more than 90% of all diabetes cases.² China is associated with the largest number of patients with diabetes and the fastest-growing diabetes prevalence rate in the world.³ A recent epidemiological survey showed that the prevalence of diabetes in Chinese adults was 12.8%⁴ and the significant increase is mainly attributed to T2DM.⁵ T2DM treatment aims to control blood glucose levels and slow down complications. Improvement in medication adherence can result in better health outcomes.⁶ According to the control criterion for the prevention and treatment of type 2 diabetes in China, the glycemic control rate of T2DM in China was low, as shown by fasting plasma glucose (FPG), 2 h postprandial plasma glucose (2hPG),

and glycated hemoglobin (HbA1c) control rates of 25.5%, 22.7%, and 19.5%, respectively.^{7,8} Poorly controlled diabetes is associated with the development of macrovascular and microvascular complications,⁹ such as cardiovascular disease,¹⁰ sudden death,¹¹ cerebrovascular disease,¹² diabetic nephropathy,¹³ diabetic retinopathy,¹⁴ and so on. Previous studies have proved that the severity of vascular complications depends on the duration and degree of hyperglycemia.^{15,16} Given the substantial clinical impact of diabetes as a risk factor for macrovascular and microvascular injury, successful management of blood glucose levels can reduce the number of vascular events.¹⁷

Non-adherence to medication therapy is the major obstacle in the management of T2DM.¹⁸ For the successful management of T2DM, medication adherence, and persistence with the treatment are crucial.¹⁹ Previous studies have confirmed that pharmacist-led interventions can improve T2DM patients' medication adherence and glycemic control.^{20–24} However, other studies have pointed out that the role of pharmacists in improving medication adherence or clinical outcomes remained controversial.^{25–27} The exact role of pharmacists in improving medication adherence needs further examination, and there are few studies related to this topic in China. In the real world, the current status of medication adherence and glycemic control in patients with T2DM in China is still unclear. Thus, this study aimed to investigate medication adherence and glycemic control in T2DM patients and evaluate the effect of pharmacist-led interventions.

Materials and Methods

Patients Enrollment

This study was a multicenter, prospective survey of T2DM outpatients conducted in 35 medical institutions (including 5 tertiary hospitals, 6 secondary hospitals, and 24 community health service centers) in Beijing, China, with Beijing Tiantan Hospital affiliated to Capital Medical University as the main investigator. Written informed consent was obtained from each patient. All data were collected between May 2020 and April 2021. Before the initiation of this study, the questionnaire, research plan, and informed consent form were reviewed and approved by the Ethics Committee of Beijing Tiantan Hospital (Approval No.: KY2020-085-02, 2020-8-23) and all participating institutions.

The following inclusion criteria were used: (1) T2DM patients (aged between 35 and 85 years) who were treated with hypoglycemic drugs for at least 6 months, (2) patients with no cognitive impairment and ability to communicate independently and participate in the research voluntarily, (3) patients with the ability to record medicine information, monitor blood glucose levels regularly, and follow-up for at least 3 months, and (4) patients that understand the questionnaire or scale after explanation and cooperate with pharmacists to complete the questionnaire. Patients who did not follow up and/or had incomplete follow-up were excluded from the analysis. The screening flow chart of enrolled patients was listed in [Figure 1](#).

Study Design

The experts of the research group designed the Questionnaire of Medication Adherence and Glycemic Control Rate of T2DM (QMAGCR) concerning the reported common factors influencing medication adherence. The QMAGCR included the following five parts (38 items): (1) demographic and sociological characteristics of the patients, (2) diabetes and medication information, (3) medication records, (4) medication adherence, and (5) behavior and lifestyle compliance.

Medication Adherence Assessment

Medication adherence was determined according to the patient's compliance with prescribed medication during the last 3 months. There were nine items with four options (score of 1–4). The answers followed Likert's four categories where 1 point and 4 points signify “never” and “always”, or the reverse. Here, the total is the sum of the scores for each question, with the highest score of 36. A higher score represents better adherence, scores of 36, 27 – < 36, and < 27 were defined as good, moderate, and poor adherence ([Supplementary Table S1](#)).

Lifestyle Compliance Assessment and Glycemic Control Criteria

A total of 9 questions were set, and the scoring standard of question options was consistent with the scoring rules of medication adherence above. (See [Supplementary Table S2](#) for more details).

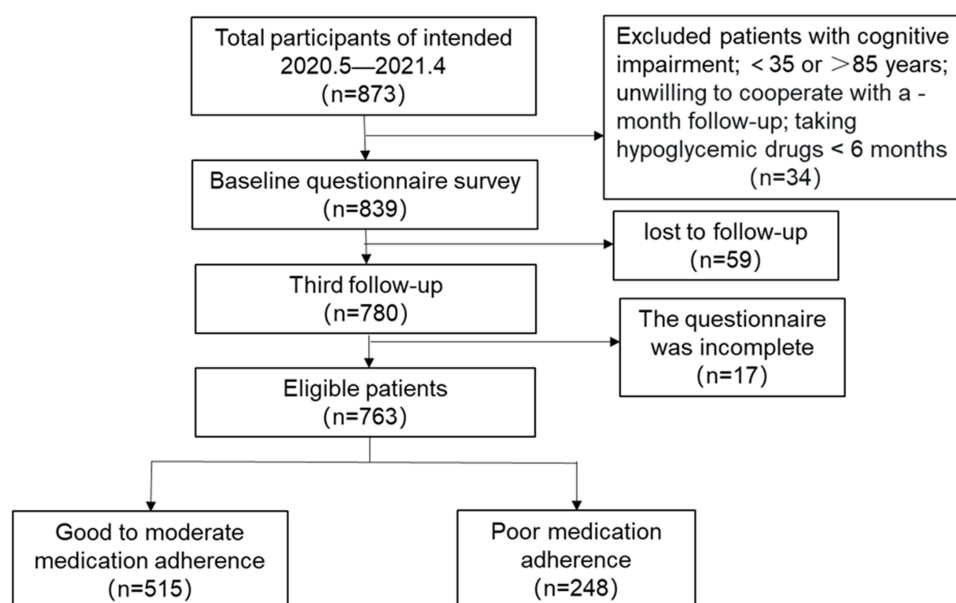


Figure 1 Screening flow chart of enrolled patients.

Fasting Plasma Glucose, 2hPG, and HbA1c levels were used to assess the glycemic control of the patients. The glycemic control criteria were according to the guidelines for the prevention and treatment of T2DM in China formulated by the diabetes branch of the Chinese Medical Association;⁸ successful glycemic control was defined as HbA1c <7% or FPG <7.0 mmol/L; the goal of 2hPG was 4.4~10 mmol/L. The results of FPG and 2hPG were based on the latest day results self-reported by the patient or the patient's laboratory test results at baseline and the third follow-up; HbA1c was obtained from the patient's laboratory test results within the last month.

Pharmacist-Led Interventions

The pharmacists involved in the study were consultant pharmacists with more than 5 years of work experience or clinical pharmacists with more than 2 years of work experience; they were fully informed and trained about the study. Pharmacists conducted baseline surveys in the form of face-to-face interviews after patients' informed consent. All patients were followed up by phone or WeChat for 3 months, and the QMAGCR was filled out at baseline and the third visit. The first survey was used as a baseline study, and three follow-up visits were conducted in the first, second, and third months after the baseline study. At the first and second follow-up visits, only any medication related problems or adjustments were recorded. Simple medication consultation and diabetes medication education were provided for patients with good adherence at baseline. Patients with moderate and poor adherence were provided with individualized pharmacist-led interventions, which included medication reconciliations, time and dosage adjustments, education on diabetes medication, proper use of insulin, medication reminders, adverse reactions and management of drugs, diet control, exercise recommendations, and so on.

Statistical Analysis

Statistical analyses were performed using Microsoft Excel and IBM SPSS Statistics 22.0. The data were plotted using GraphPad Prism v5.0. Enumeration data were statistically described by frequency and rate (%), while the measurement data were expressed as the mean \pm SD. Descriptive statistics, chi-square (χ^2) test, *t*-test, and rank sum test, were used to evaluate the results. Results were considered statistically significant if the *p* value < 0.05.

Results

Demographic and Sociological Characteristics of Patients

A total of 763 T2DM patients were included in the study, with 363 male (47.58%) and 400 female (52.42%). The average age of the patients was 63.26 ± 11.89 years. There were 488 cases (63.96%) that had diabetes for more than 5 years,

while 266 cases (34.86%) received hypoglycemic drugs for more than 10 years. Among 763 patients, 276 (36.17%) patients got more than 3 kinds of combined chronic diseases, and 455 (59.63%) patients received more than 2 categories of hypoglycemic drugs. The demographic and sociological characteristics of the patients were summarized in Table 1.

Medication Adherence

Baseline and 3-month follow-up investigations were considered for pre- and post-intervention, respectively. A paired sample *t*-test was used to compare medication adherence scores before and after the intervention. The number of patients

Table 1 Demographic and Sociological Characteristics of T2DM Patients

Demographics	Grouping	No. of Patients (%), n=763
Age (years)	<45	54 (7.08)
	45–<60	214 (28.05)
	≥60	495 (64.87)
Gender	Male	363 (47.58)
	Female	400 (52.42)
Residence	Urban	681 (89.25)
	Rural	82 (10.75)
Level of education	Primary	234 (30.67)
	Secondary	358 (46.92)
	University degree or above	171 (22.41)
BMI ^a (kg/m ²)	<24	264 (34.60)
	24–<28	327 (42.86)
	≥28	172 (22.5)
Smoking	Yes	136 (17.82)
	No	627 (82.18)
Drinking	Yes	148 (19.40)
	No	615 (80.60)
Marital status	Married	678 (88.86)
	Single	95 (12.45)
Working status	Be on the job	184 (24.12)
	Retirement	518 (67.89)
	Others ^b	61 (7.99)
Monthly income (dollar)	<700	417 (54.65)
	700–1400	270 (35.39)
	>1400	76 (9.97)
Medical payment	Self-paying	29 (3.80)
	Medical Insurance	734 (96.20)
The convenience of access to medicines	Convenient	727 (95.28)
	Inconvenient	36 (4.72)
Combined chronic diseases	≤2	487 (63.83)
	≥3	276 (36.17)
Duration of diabetes (years)	≤5	275 (36.04)
	>5	488 (63.96)
Blood glucose control levels	Known	443 (58.06)
	Unknown	320 (41.94)
Participated in diabetes education	Yes	345 (45.22)
	No	418 (54.78)
Number of hypoglycemic drugs used	1	308 (40.37)
	≥2	455 (59.63)
Duration of drug used (years)	≤1	106 (13.89)
	2–5	240 (31.45)
	6–10	151 (19.79)
	>10	266 (34.86)

Notes: ^aBMI, body mass index. Others^b, farming, unemployed, school.

with good, moderate, and poor adherence at baseline was 261 (34.21%), 254 (33.29%), and 248 (32.50%), respectively. Post-intervention, the patients with good adherence increased (261 (34.21%) to 298 (39.06%)), while with poor adherence decreased (248 (32.5%) to 187 (24.5%)); the average score of medication adherence increased significantly ($p < 0.001$) from 27.846 ± 4.185 to 29.831 ± 7.065 (Table 2).

Glycemic Control of T2DM Patients

Before the intervention, the number (percentage) of patients with FPG between 4.4 and 7.0 mmol/L and HbA1c < 7% were 323 (42.33%) and 184 (24.12%), respectively; 318 cases (41.68%) reached the goal of 2hPG between 4.4 and 10 mmol/L. Patients were divided into four categories according to blood glucose control qualified and unqualified, before and after the intervention, and the chi-square test was used for comparison between groups. The results showed statistically significant differences to that of post-intervention ($P < 0.05$), where the number of patients with FPG, 2hPG, and HbA1c reaching the standard was 409 (53.06%), 372 (48.75%), and 223 (29.23%), respectively (Table 3).

Lifestyle Compliance of T2DM Patients

After the pharmacist-led interventions, the number of patients with a lifestyle compliance score of more than 27 increased from 242 to 299, and the average score of patients' lifestyle compliance increased from 22.82 ± 5.29 to 27.85 ± 3.54 . An Independent sample *T*-test was used to compare the changes in lifestyle compliance scores before and after pharmacists' intervention, and the results were a significant statistical difference ($p < 0.001$) (Figure 2).

Factors Influencing Medication Adherence

Patients were divided into 2 groups, one was with good to moderate adherence and the other was patients with poor adherence. Our results show that gender, age, BMI, smoking, monthly income, blood glucose monitoring, duration of hypoglycemic drug used, use of medications empirically, following the doctor's advice to visit, and lifestyle compliance were the significant influencing factors ($p < 0.05$) according to univariate analysis (Supplementary Table S3). To reduce the effect of confounding factors, the factors identified above were further analyzed by binary logistic regression. As

Table 2 Comparison of Medication Adherence of Patients Pre- and Post-Intervention

Time	Good Adherence ^a	Moderate Adherence	Poor Adherence	Average Adherence Score	t-value	p value
Pre-Intervention	261 (34.21)	254 (33.29)	248 (32.50)	27.846±4.185	-10.566	<0.001
Post-Intervention	298 (39.06)	278 (36.44)	187 (24.50)	29.831±7.065		

Notes: ^an (%) for proportions. The number of patients with good, moderate, and poor adherence pre- and post-intervention were compared. The adherence scores of 763 patients pre- and post-intervention were compared by t-test to evaluate the effect of the pharmacist-led intervention.

Table 3 Comparison of the Glycemic Control of T2DM Patients Pre- and Post-Intervention

Items	Reach the Standard	Pre-Intervention n (%) ^a	Post-Intervention n (%)	χ^2	p value
FPG ^b	Yes	323 (42.33)	409 (53.60)	19.419	<0.001
	No	440 (57.67)	354 (46.40)		
2hPG	Yes	318 (41.68)	372 (48.75)	7.714	0.005
	No	445 (58.32)	391 (51.25)		
HbA1c	Yes	184 (24.12)	223 (29.23)	5.096	0.024
	No	579 (75.88)	540 (70.77)		

Notes: ^an (%) for proportions; ^bFPG, fasting plasma glucose; 2hPG, 2 h postprandial plasma glucose; HbA1c, glycosylated hemoglobin. A total of 763 patients were divided into two groups according to the number of patients with or without reaching the standard of FPG, 2hPG, and HbA1c, respectively. The Chi-square test was used to compare the change in the number of people pre- and post-intervention.

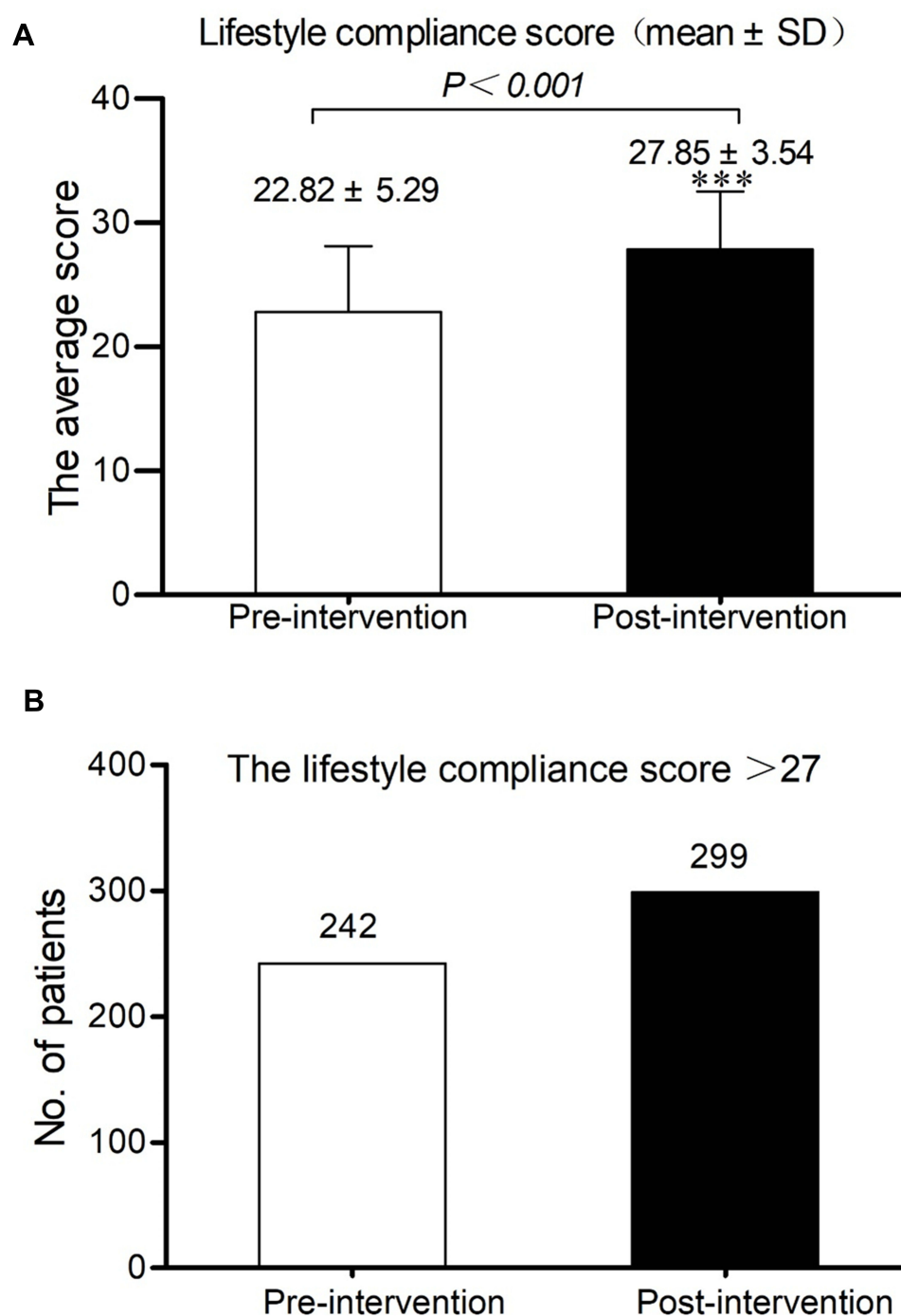


Figure 2 Comparison of the lifestyle compliance pre- and post-intervention. **(A)** Lifestyle compliance score comparison (t-test, $p < 0.001$); **(B)** Changes in the number of patients with a lifestyle compliance of score more than 27 pre- and post-intervention.

Note: ***Indicates $P < 0.001$.

shown in Table 4, BMI, use of medications empirically, following the doctor's advice to visit, and lifestyle compliance were the factors showing a significant influence on medication adherence after controlling other variables. Use of medications empirically (occasionally (OR 3.066, 95% CI 2.069–4.543); often (OR 2.984, 95% CI 1.107–8.044)), occasionally following the doctor's advice to visit (OR 2.129, 95% CI 1.079–4.202) and lifestyle compliance score of less than 18 (OR 2.835, 95% CI 1.094–7.346) were positively correlated with the risk of poor medication adherence. BMI displayed a negative effect on the risk of poor adherence (OR 0.643, 95% CI 0.437–0.945).

Table 4 Binary Logistic Regression Analysis of Risk Factors of Medication Adherence

Characteristic	OR	95% CI	p value ^a
Gender (set "male" = 0)			
Female	0.872	[0.602, 1.263]	0.469
Age	0.977	[0.950, 1.005]	0.109
Age group (set "<45" = 0)			
45– <60	0.829	[0.364, 1.885]	0.654
≥60	1.349	[0.441, 4.129]	0.600
BMI	1.007	[0.998, 1.107]	0.123
BMI group (set "<24" = 0)			
24– <28	0.643	[0.437, 0.945]	0.025
≥28	0.915	[0.579, 1.446]	0.703
Smoking (set "No" = 0)			
Yes	1.401	[0.882, 2.226]	0.153
Monthly income (set "<700" = 0)			
700–1400	0.724	[0.500, 1.049]	0.088
>1400	0.812	[0.439, 1.503]	0.508
Duration of drug used (set "≤1" = 0)			
2–5	1.319	[0.768, 2.267]	0.316
6–10	1.503	[0.834, 2.710]	0.175
>10	1.145	[0.649, 2.019]	0.640
Monitor blood glucose regularly (set "No" = 0)			
Yes	0.996	[0.664, 1.494]	0.986
Use of medications empirically (set "never" = 0)			
Occasionally	3.066	[2.069, 4.543]	<0.001
Often	2.984	[1.107, 8.044]	0.031
Following the doctor's advice to visit (set "Always execution" = 0)			
Frequent execution	1.229	[0.667, 2.267]	0.509
Occasional execution	2.129	[1.079, 4.202]	0.029
No execution	1.375	[0.444, 4.261]	0.581
Lifestyle compliance score (set ">27" = 0)			
18–27	1.231	[0.737, 2.056]	0.426
<18	2.835	[1.094, 7.346]	0.032
Constant term	0.793		0.790

Notes: ^ap value by binomial logistic regression test p = significance of different tests.

Abbreviations: OR, odds ratio; CI, confidence interval.

According to the logistic regression analysis, the adherence probability test result variables were generated, and the probability result variables were drawn into receiver operating characteristic (ROC) curves to predict adherence results. The area under the ROC curve was 0.716 (range 0.7–0.9), indicating the model with good predictive value. At the same time, the model showed a certain explanatory ability since the significance *p-value* of the model was <0.001. Furthermore, the model was also found to display high prediction accuracy (correct prediction samples accounted for 72.1% of all the samples).

Discussion

Medication adherence directly influences glycemic control and clinical consequences, with suboptimal glycemic control leading to vascular complications. Non-adherence to medication therapy remains a challenge to achieving optimal clinical outcomes. Our study provides data for getting the whole picture of the current status of medication adherence and glycemic control in patients with type 2 diabetes in Beijing. To the best of our knowledge, this was the first prospective study from Beijing that proved the value of pharmacist-led interventions on medication adherence in T2DM

patients. Although a few studies had assessed adherence in T2DM patients, they were either cross-sectional studies,^{28–31} or retrospective studies^{32,33} and none of them had to consider the effect of pharmacist-led interventions. Our findings highlighted the importance of pharmacist-led interventions in T2DM patients, which were consistent with those of previous studies.^{34,35}

We found that the overall glycemic control with HbA1c < 7% at baseline was 24.12%, higher than that reported in a previous study in China, where the control rate of HbA1c was 19.5%.⁷ In 2011, a multicenter cross-sectional study of 238,639 T2DM patients in China showed that 31.78% of the patients had achieved the goal of HbA1c < 7.0%.²⁸ These findings illustrated that there was no significant improvement in glycemic control of Chinese T2DM patients over the past 10 years, although the variations between studies can be partially explained by differences in sample size, regional distribution, and study design. Therefore, it is urgently required to strengthen the interventions on medication adherence of T2DM patients and improve glycemic control. Non-adherence to medication can result in poor glycemic control,³⁶ as also observed in our study. Pharmacist-led interventions should be encouraged in the treatment of non-adherence T2DM patients, and this strategy should be further promoted and applied. With the implementation of graded diagnosis and treatment political strategy in China, chronic disease management is sinking into the community. How to take advantage of this opportunity, give full play to the professional advantages of family pharmacists, and improve the medication adherence and glycemic control of T2DM patients deserves our thinking.

The factors leading to non-adherence are complex and can be divided into the patient, social and economic, medication treatment, health providers, and health system-related factors.³⁷ Our study found that BMI, use of medications empirically, following the doctor's advice to visit, and lifestyle compliance were independent risk factors of non-adherence. Obesity and overweight are two important risk factors for T2DM, and changes in these factors could contribute to the prevalence of total factors.³⁸ A study in the USA found that adults with T2DM who lost weight had better medication adherence as compared to those who gained weight.³⁹ However, our study found that the risk of poor adherence was lower in patients with BMI between 24 and 28 kg/m² than those with a BMI of <24 kg/m². There could be several reasons for this finding. First, the prevalence of obesity and overweight increased greatly in China with a mean annual rate of 5.8%, and obesity contributes to the rise of diabetes.⁴⁰ This trend may be related to the fact that people tend to start taking hypoglycemic drugs when they realize that obesity has greatly affected their health. Second, national diabetes control education is becoming increasingly popular, especially for obese people. The more education this group received, the higher the adherence. Third, some types of hypoglycemic drugs can reduce body weight. Hence, obese patients with diabetes are more willing to accept hypoglycemic drug treatment, and their adherence is relatively high. A study in Papua New Guinea found that age was a risk factor for non-adherence in T2DM patients.³⁶ Our study found no significant effect of age on medication adherence. This could explain by most of the patients in this study being between 60 and 75 years, and the age distribution was uneven.

Logistic regression in our study showed that the patients who always take medicines empirically and occasionally visit doctors were associated with poor medication adherence. These findings suggest that strategies that reduce the use of medications empirically, increase following doctor's advice to visit, and improve lifestyle compliance, may improve medication adherence.

There were limitations of this study: (1). First, we excluded patients who were unwilling to participate in the study, which may have contributed to the bias in the study population. (2). Second, adherence assessment questions were based on patients' subjective recollection, and may be biased. In addition, the blood glucose measurement results of some patients were based on self-report and were not validated through biomarkers or other checks, which would affect the accuracy of the study results. (3). Third, there may be some deviation in assessing overall glycemic control when the HbA1c level is <7.0%. Glycemic control should include FPG, non-FPG, and HbA1c.⁸ In our study, although we collected FPG, 2hPG, and HbA1c, HbA1c <7.0% was selected as the overall glycemic control. HbA1c is the best index used to prove the effect of glycemic control in clinical trials, and can reflect the average blood sugar level in the last three months.⁸ Both the American Diabetes Diagnosis and Treatment Guidelines and Chinese Diabetes Diagnosis and Treatment Guidelines⁸ recommend that the control target value of HbA1c in adult non-gestational diabetes patients is <7.0%. Although there are limitations in the method of assessing overall glycemic control, a consistent threshold is preferred for comparison throughout the study. (4). Fourth, the study focused on statistical significance and was unable to

determine whether differences in outcomes represented minimal clinically important differences. Finally, there may be unmeasured confounding variables in our study, which could bias the results. For example, we did not survey information about the patient's drug and medical costs, which were found to be financial barriers to medication adherence.⁴¹

Conclusion

The medication adherence and glycemic control of T2DM patients in Beijing were currently suboptimal, and they could be significantly improved by pharmacist-led interventions. Pharmacist-led interventions should be encouraged in the management of T2DM. Our findings suggest that strategies that reduce the use of medications empirically, increase following doctor's advice to visit and improve lifestyle compliance, may improve medication adherence. Given that this study was based on patient self-reported adherence and blood glucose monitoring results, the recall bias with self-reported results needs further objective data to verify.

Abbreviations

T2DM, Type 2 Diabetes Mellitus; FPG, Fasting plasma glucose; 2hPG, 2-h postprandial plasma glucose; HbA1c, Glycated hemoglobin; QMAGCR, Medication Adherence and Glycemic Control Rate of T2DM; BMI, Body mass index.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author Zhigang Zhao upon reasonable request.

Ethics Approval and Informed Consent

The research was in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of Beijing Tiantan Hospital, the reference number KY2020-085-02. Informed written consent has been obtained from each patient after a full explanation of the purpose and nature of all procedures used.

Consent for Publication

All data generated or analyzed during this study are included in this published article and [Supplementary Tables](#). We confirm that the details of any tables, figures, or data can be published and that the person(s) providing consent have been shown the article contents to be published.

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Disclosure

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