

# Patient-Reported Outcomes Following the Use of Jiang Tang San Huang Tablets in Type 2 Diabetes Mellitus: A Retrospective Cohort Study in a Chinese Population

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**Purpose:** We aimed to assess the efficacy of the Jiang Tang San Huang (JTSH) tablet for the treatment of patients with type 2 diabetes mellitus (T2DM).

**Methods:** All data for this retrospective cohort study were acquired from the outpatient clinic database of our institution, and all enrolled patients received JTSH tablet for at least two months. Overall, 147 patients were included in the analysis. The primary outcome was patient-reported outcomes on the efficacy of the JTSH tablets using a questionnaire survey. Correlation analysis evaluated the duration of JTSH tablet administration and glycemic control in patients with T2DM. The secondary outcome measures included: changes in glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), 2-hour postprandial blood glucose, homeostasis model assessment of insulin resistance index (HOMA-IR) and homeostasis model assessment of  $\beta$ -cell function (HOMA- $\beta$ ) after 2 months of treatment with JTSH tablets.

**Results:** Overall, 120 patients (81.63%) reported a JTSH tablet treatment satisfaction score of  $\geq 60$  points, and believed that JTSH tablets had satisfactory hypoglycemic effects and could improve symptoms. The average duration of JTSH tablet treatment was  $2.57 \pm 1.45$  years. Overall, 111 patients achieved good blood glucose control, while 36 patients had poor glycemic control. Multivariate logistic regression model analysis showed that taking JTSH tablets for 1 year might reduce the risk of poor hypoglycemic effect by 17.00% (Risk ratio=0.830, 95% confidence interval:0.578, 1.021,  $P=0.066$ ). Compared with the baseline data, the levels of HbA1c, FPG and HOMA-IR decreased significantly and HOMA- $\beta$  levels increased significantly ( $P<0.05$ ).

**Conclusion:** Good blood glucose control may be positively correlated with the duration of JTSH tablets administration. Patients with T2DM were satisfied with the anti-diabetic effects of JTSH tablets, which can significantly reduce blood glucose and insulin resistance, and improve the function of islet cells.

**Keywords:** type 2 diabetes mellitus, Jiang Tang San Huang tablet, patient-reported outcomes, blood glucose control, multiple logistic regression

## Introduction

Diabetes is a chronic metabolic disorder that impacts the quality of patients' life. In 2021, the International Diabetes Federation officially announced that the global prevalence of diabetes was 10.5% among individuals aged 20–79 years, with 536.6 million people living with the disease, among which China had the highest prevalence of approximately 26.23% (140.9 million).<sup>1</sup> Type 2 diabetes mellitus (T2DM) accounts for more than 90% of all diabetes cases, with its prevention and

treatment being a prevalent social concern. At present, the treatment of T2DM and its complications mainly depends on antidiabetic drugs; however, several patients taking antidiabetic agents experience adverse effects.<sup>2,3</sup> In addition, the clinical hypoglycemic effect from these agents is not adequate, nor can they delay the progression of diabetic complications.<sup>4</sup>

In China, Chinese herbal medicine (CHM) is widely used in managing various acute and chronic conditions, including early diabetes<sup>5,6</sup> as well as in the prevention and treatment of its complications.<sup>7</sup> Due to positive outcomes experienced by patients taking CHM therapies, and the increased availability of the prescriptions, CHMs are increasingly being used globally.<sup>8</sup> The application of Chinese medicine for the management of T2DM or its complications is widespread in China because it is believed to reduce the risk of disease progression to type 2 diabetic nephropathy and increase the likelihood of a return to normoglycemia.<sup>9–11</sup> In addition, the use of CHM is frequently determined by the patient's beliefs rather than a physician's recommendation. Previous studies have found that patients who were unsatisfied with conventional therapy were more likely to turn to complementary therapies.<sup>12,13</sup>

The Endocrinology Committee of the World Federation of Chinese Medicine Societies developed the International CHM Guidelines to provide standardized diabetes diagnosis and treatment recommendations for global use.<sup>14</sup> However, the efficacy standards of hypoglycemic drugs are not completely suited for the efficacy evaluation of CHM. Currently, the evaluation system of CHM in the treatment of T2DM is not standardized or validated, which raises questions about the clinical hypoglycemic efficacy provided by these agents.<sup>15,16</sup>

Patient-reported outcomes (PROs) have gained prominence in patient management and clinical decision-making since their inception in the 1980s.<sup>17</sup> PROs are direct reports from patients about how they feel or are functioning in response to a health condition and its therapy without interpretation by a healthcare professional. Patients can relate to symptoms, signs, functional status, perceptions or other aspects of care such as convenience and tolerability.<sup>18</sup> Recently, PROs have gained prominence in the management and clinical decision-making of patients with T2DM<sup>19</sup> or cancer.<sup>20–22</sup> Studies have confirmed the effectiveness of CHM in the treatment of breast cancer,<sup>23</sup> chronic obstructive pulmonary disease,<sup>24</sup> irritable bowel syndrome,<sup>25</sup> and other diseases based on PRO related scales. However, there is currently no PRO scale for evaluating the efficacy of CHM treatment in patients with T2DM.<sup>17,19</sup>

Our team is committed to the clinical application and scientific research of CHM in managing T2DM and its complications for nearly 30 years, and has proposed a method of lowering blood glucose by removing heat and removing blood stasis.<sup>26,27</sup> Jiang Tang San Huang (JTSH) tablet is the core prescription, which is an institutional preparation approved by the Guangdong Pharmaceutical and Food Administration (No. Z20071185).

In 2018, Professor Li evaluated approximately 549 patients with T2DM receiving treatment with JTSH tablets from the outpatient departments of the First Affiliated Hospital of Guangzhou University of Chinese Medicine. In this study, the results of patients were collected according to the frequency of visits, purpose of visits, main symptoms, hypoglycemic drugs, hypoglycemic efficacy and questionnaire survey, and the hypoglycemic efficacy of the JTSH tablets was primarily introduced to readers from the perspective of patients.

## Materials and Methods

### Study Design

We conducted a retrospective cohort study among outpatient departments in the First Affiliated Hospital of Guangzhou University of Chinese Medicine. All data were obtained from the outpatient database of our hospital, and extracted by trained clinical doctors. We began to collect patient information in January 2020 and conducted telephonic interviews and outpatient follow-ups on patients' administration of JTSH tablets and their blood glucose control. The medicinal components of the JTSH tablet are listed in [Table 1](#).

Using a 2-tailed test ( $\alpha=0.05$ ,  $\beta=0.20$ ) and 10% dropout, the Power Analysis and Sample Size software estimated the sample size of approximately 126 cases.

### Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).<sup>28</sup> The Research Ethics Committee of the First Affiliated Hospital of Guangzhou University of Chinese Medicine approved the study (approval

**Table 1** Composition of the Jiang Tang San Huang Tablet

Latin Name	Chinese Name	Dosage
<i>Prunus persica</i> (L.) Batsch	Taoren	9–12 g
Ramulus Cinnamomi	Guizhi	6–12 g
Radix et Rhizoma Rhei	Dahuang	6–12 g
Thenardite	Xuanmingfen	3–6 g
Astragali Radix	Huangqi	30 g
<i>Rehmannia glutinosa</i>	Dihuang	12–15 g
<i>Ophiopogon japonicus</i>	Maidong	12 g
Scrophulariae Radix	Xuanshen	12–15 g
Glycyrrhizae Radix et Rhizoma	Gancao	3–6 g

number: ZYYECK [2020] 135). Furthermore, considering that the questionnaire was completed during the health education process for patients newly diagnosed with T2DM, the Ethics Committee approved that no informed consent was required.

## Inclusion Criteria

The inclusion criteria were as follows: patients who (1) met the diagnostic criteria of T2DM proposed by the 1990 World Health Organization's Committee of Experts on Diabetes; (2) were aged between 18 and 85 years; (3) visited an outpatient clinic from 1 January 2018 to 30 December 2018; (4) visited the clinic at least twice, and used JTSH tablets for  $\geq 2$  months; (5) had glycated hemoglobin (HbA1c) values in the range of 6.5%-12%, had already received oral hypoglycemic drugs or subcutaneous insulin therapy, or a combination of both or neither.

## Exclusion Criteria

Patients were excluded if they: (1) had other specific types of diabetes, including gestational diabetes; (2) had experienced acute complications of diabetes (eg, hyperosmolar coma, diabetic ketoacidosis, and diabetic lactic acidosis); (3) had objections to the collection of personal information or other relevant data; and (4) had serious heart, liver, kidney, brain or other complications, or had other serious primary diseases that require urgent treatment.

## Participants

Among 549 patients with T2DM in 2018, 245 patients visited the clinic only once; 140 patients taking JTSH tablets less than 2 months. Overall, 164 patients met the inclusion criteria, and 4 patients were excluded based on serious complications and 13 patients did not participate in the questionnaire survey.

## Data Collection and Definitions

In this retrospective cohort study, we recorded baseline data of patients including age, sex, weight, height, blood parameters (including HbA1c, oral glucose tolerance test, islet function test), past medical history, as well as questionnaire items for JTSH tablet treatment in patients with T2DM.

The questionnaire items are shown in Table 2. By asking patients to fill out a questionnaire, we obtained the patients' reasons and satisfaction scores relating to the hypoglycemic effect of JTSH tablet, as well as their current hypoglycemic regimens and subjective evaluations of JTSH tablet and antidiabetic drugs. In addition, we recorded details of the patient's diet and exercise.

**Table 2** Questionnaire Items for the Treatment of T2DM with JTSH Tablet

Purpose of visit	1. Cure diabetes; 2. Continue treating diabetes, improve self-discomfort symptoms, or reduce the side effects of Western hypoglycemic medicine.
Reason for choosing CHM	1. Believe that Chinese medicine can cure the root cause; 2. Friends recommend CHM because of its curative effects; 3. CHM has few side effects; 4. Willing to try various methods.
Efficacy satisfaction score (1–100 points)	The hypoglycemic effect of traditional Chinese medicine is very satisfactory (score $\geq 80$ ); CHM has a specific hypoglycemic effect; however, the onset is slow; it also regulates the body'' (score $\geq 60$ ); Chinese medicine is ineffective in lowering blood glucose (score $< 60$ ).
Current hypoglycemic regimen(s) and efficacy	(1) Insulin; (2) Western medicine; (3) CHM containing JTSH tablet; The efficacy on glucose control: fasting and 2-hour postprandial blood sugar status.
Advantages	1. The anti-diabetic efficacy of CHM is satisfactory; 2. The CHM regulates the body; 3. It is safe and has no side effects.
Disadvantages	1. The hypoglycemic effect is not as good as that of Western medicine (slow or unstable); 2. It is difficult to prepare the medicine; 3. It is expensive; (4) The taste of CHM is horrible.
Western medicine evaluation	1. Efficacy 2. Side effects.
Diet & Exercise	Self-management of diet and exercise.

**Abbreviations:** JTSH tablet, Jiang Tang San Huang tablet; CHM, Chinese herbal medicine; T2DM, Type 2 diabetes mellitus.

We calculated the duration of JTSH tablet treatment for each enrolled patient based on information extracted from medical record system or from a telephone follow-up. We focused on analyzing the influencing factors of blood glucose control in patients with T2DM who had a duration of JTSH tablet administration of more than 2 months.

All the data were updated as of 30 August 2021. By December 2021, those whose information had not been obtained through telephone follow-up or the electronic medical record system were considered lost to follow-up.

## Calculation of Parameters

The Body mass index (BMI) is a statistical index that provides an estimate of body fat of any age; it is calculated as  $BMI = \text{weight (in kg)} / \text{height}^2 \text{ (in m}^2\text{)}$ .<sup>28</sup>

Homeostatic model assessment (HOMA) is a method used to quantify insulin resistance

(HOMA-IR) and  $\beta$ -cell function (HOMA- $\beta$ ). We calculated HOMA- $\beta$  and HOMA-IR by the formulas:  $HOMA-\beta = 20 \times FINS / (FPG - 3.5)$ ;  $HOMA-IR = (FPG \times FINS) / 22.5$ .<sup>29</sup>

## Data Quality Assurance and Management

The statisticians responsible for this study's statistical work set up a "dedicated database" and input all the experimental data. The statistical professionals were blinded to the patient's information to reduce assessment bias.

The database of our hospital's electronic medical record system was used for data extraction, and data entry was conducted secondarily. The data was independently entered by 2 people and was checked and corrected item by item to ensure the accuracy of the input data.

## Outcomes

The primary outcome point was the satisfaction score of patients with T2DM treated with JTSH tablets and the correlation analysis between the time of JTSH tablet administration and glycemic control in patients with T2DM.

The secondary outcome measures were blood parameters such as HbA1c, fasting plasma glucose (FPG), 2-hour postprandial blood glucose (2hPG), HOMA-IR, and HOMA- $\beta$ .

Evaluation of hypoglycemic efficacy was based on the “Guidelines for Clinical Research of New Chinese Medicines”.<sup>30</sup>

## Statistical Analysis

Statistical analyses were performed using the statistical software packages R (The R Foundation for Statistical Computing, Vienna, Austria) and Empower States (<http://www.empowerstates.com>, X & Y Solutions, Inc. Boston, MA, USA). All tests were 2-sided, with the statistical significance level set at 0.05.

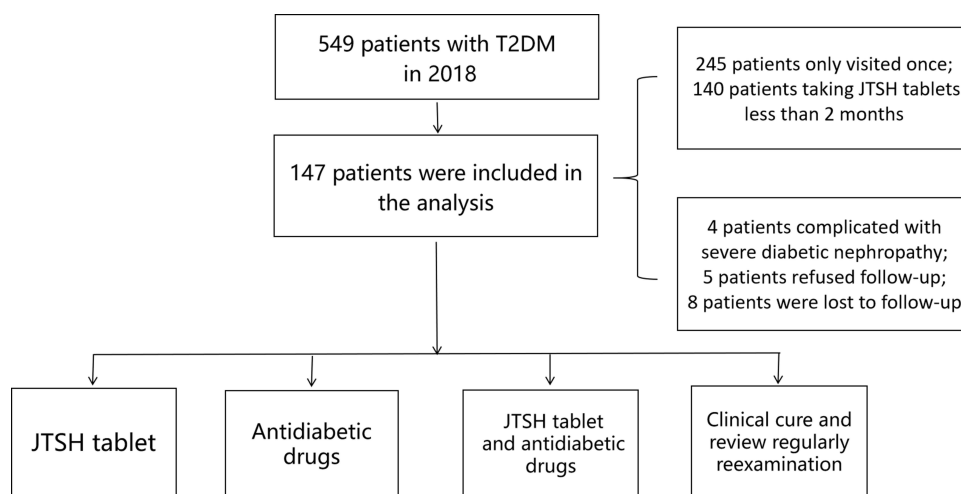
Regarding demographic and clinical characteristics at baseline, quantitative variables were reported as mean  $\pm$  standard deviation (SD) and qualitative variables as frequencies and percentages. HbA1c, FBG, and 2hPG levels are reported as mean  $\pm$  SD. Due to missing laboratory data for some patients, we replaced missing data with multiple imputations.

In the analysis, we also performed correlation analysis between the duration of JTSH tablet administration and glycemic control in patients with T2DM. First, through spline smoothing, we confirmed the positive correlation between taking JTSH tablet and good blood glucose control. Further, we constructed a multivariate logistic regression model I by adjusting all variables such as sex, age, BMI, diet and exercise, and adjusted for the variable of diet and exercise to conduct the multivariate logistic regression model II. Finally, we estimated the relative risk (RR) and 95% confidence intervals (CIs) using Poisson regression and Bootstrap re-sampling (times = 500).

## Results

In December 2021, 147 patients participated in the questionnaire survey, who were included in the statistical analysis. The loss to follow-up rate was 8.16%. The screening flow chart of this study population is shown in Figure 1.

Demographic and clinical patient characteristics are presented in Table 3. The mean patient age was  $53.58 \pm 13.21$  years (range = 21–82 years), and 81 (55.10%) were female. The mean BMI and duration of diabetes were  $23.26 \pm 3.68$  kg/m<sup>2</sup> and  $7.47 \pm 6.33$  years, respectively. Regarding past medical history, 25 patients had hypertension, 20 had dyslipidemia, and 8 had coronary heart disease. The mean duration of treatment with JTSH tablets was  $2.57 \pm 1.45$  years. Patients under the age of 60 years accounted for 64.63%; overall, 55 patients of T2DM were diagnosed for the first time.



**Figure 1** Flowchart of this study.

**Abbreviations:** T2DM, type 2 diabetes mellitus; JTSH tablets, Jiang Tang San Huang tablets.

**Table 3** The Distribution of Clinical Conditions of JTSH Tablet Users

	<b>N (%) / Mean <math>\pm</math> SD</b>
N	147
Age(years)	53.58 $\pm$ 13.21
Sex	
Male	69 (46.7%)
Female	78 (55.10%)
Weight(kg)	62.96 $\pm$ 12.19
BMI (kg/m <sup>2</sup> )	23.26 $\pm$ 3.68
Diabetes course(year)	7.90 $\pm$ 6.87
JTSH tablet(year)	2.57 $\pm$ 1.45
Past medical history (N)	
Hypertension	25
Coronary heart Disease	8
Dyslipidemia	20

**Note:** Continuous variables reported as the mean  $\pm$  SD.

**Abbreviations:** JTSH tablets, Jiang Tang San Huang tablets; BMI, body mass index.

The shortest and longest duration following diagnosis was 1 month and 30 years, with 44 (29.93%) patients living with the condition for more than 10 years.

## Patient-Reported Outcomes

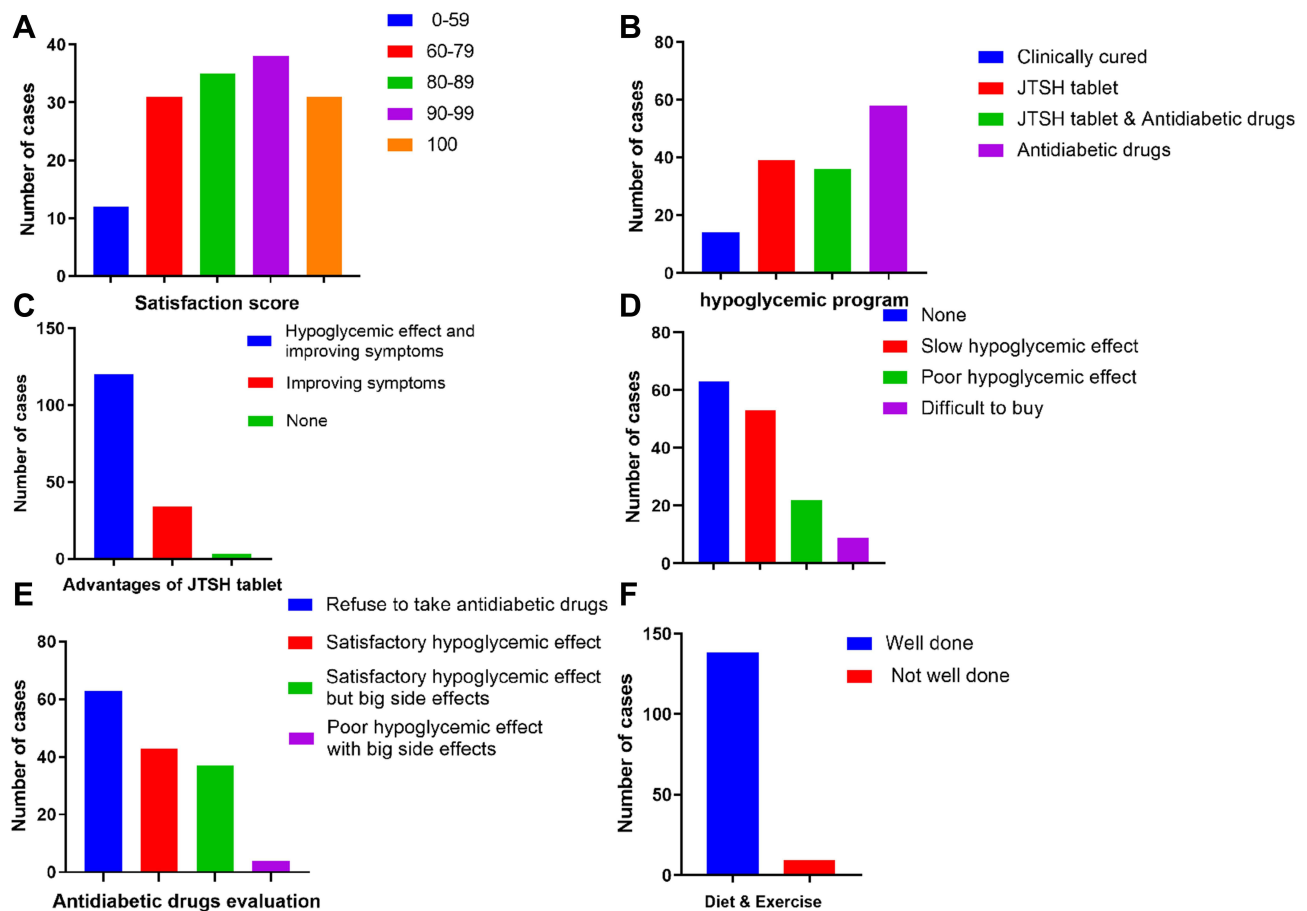
The survey results showed that the reasons for choosing treatment with JTSH tablets were varied: 33.33% of patients believed that JTSH tablets could cure T2DM, and 66.67% chose JTSH tablets to treat T2DM, prevent or delay disease-related complications and improve symptoms.

In the questionnaire survey, 135 patients scored  $\geq 60$  points in satisfaction with the efficacy of JTSH tablet in the treatment of T2DM. The scores of 35 patients were 80–89 points and 38 scored 90–99 points. There were 31 patients with 100 points, among whom, 14 patients were clinically cured, and they had the highest satisfaction with JTSH tablet treatment. However, 12 patients had a satisfaction score of  $<60$  points, indicating that they were not satisfied with the antidiabetic effect of JTSH tablets (Figure 2A).

According to the results of the questionnaire, the current hypoglycemic programs of the selected patients were as follows: (1) 39 (26.53%) cases of diabetes mellitus were controlled by JTSH tablets; (2) 14 (9.52%) patients were clinically cured after taking JTSH tablets; (3) 36 cases were treated with JTSH tablets combined with antidiabetic drugs; and (4) 58 patients discontinued JTSH tablet treatment, of which 38 had to discontinue JTSH tablets because they could not afford it during the new coronavirus disease pandemic (Figure 2B).

In addition, we achieved glycemic control in all patients. Notably, 111 patients had good blood glucose control, while 36 patients had poor glycemic control. Among the 36 patients with poor blood glucose control, 15 patients were treated with JTSH tablets and 21 received antidiabetic drugs.

Compared with antidiabetic drugs, the survey respondents believed that the advantages of JTSH tablets in treating T2DM were as follows: (1) 120 (81.63%) patients believed that Chinese medicine had satisfactory hypoglycemic effects and could improve symptoms; and (2) 24 (16.33%) patients believed that the primary role of JTSH tablet was to improve symptoms and prevent the occurrence of side effects; 3 (2.04%) patients believed that JTSH tablet had no therapeutic



**Figure 2** Representations of the results of the questionnaire items. **(A)** Satisfaction of 147 patients' with JTSH tablets treatment for T2DM. **(B)** The hypoglycemic regimens administered to the enrolled patients. **(C)** Evaluation of the advantages of JTSH tablets for treating of T2DM by lowering blood sugar or improving symptoms in 147 patients. **(D)** A total of 147 patients evaluated the disadvantages of JTSH tablets for the treatment of T2DM. **(E)** Evaluation of the hypoglycemic effect of antidiabetic drugs in 147 patients. **(F)** Evaluation of diet and exercise done well or not of 147 patients.

**Abbreviations:** JTSH tablets, Jiang Tang San Huang tablets; T2DM, type 2 diabetes mellitus.

advantage (Figure 2C). Furthermore, we determined that the most frequently improved symptoms were fatigue, insomnia, anorexia, constipation and emotional anxiety.

As for the disadvantages of JTSH tablets in treating T2DM, 53 patients recognized the antidiabetic effect of JTSH tablets appeared slowly; 22 patients thought that JTSH tablet had poor hypoglycemic effect and 9 patients reported that the difficulty of buying drugs was most important concern (Figure 2D).

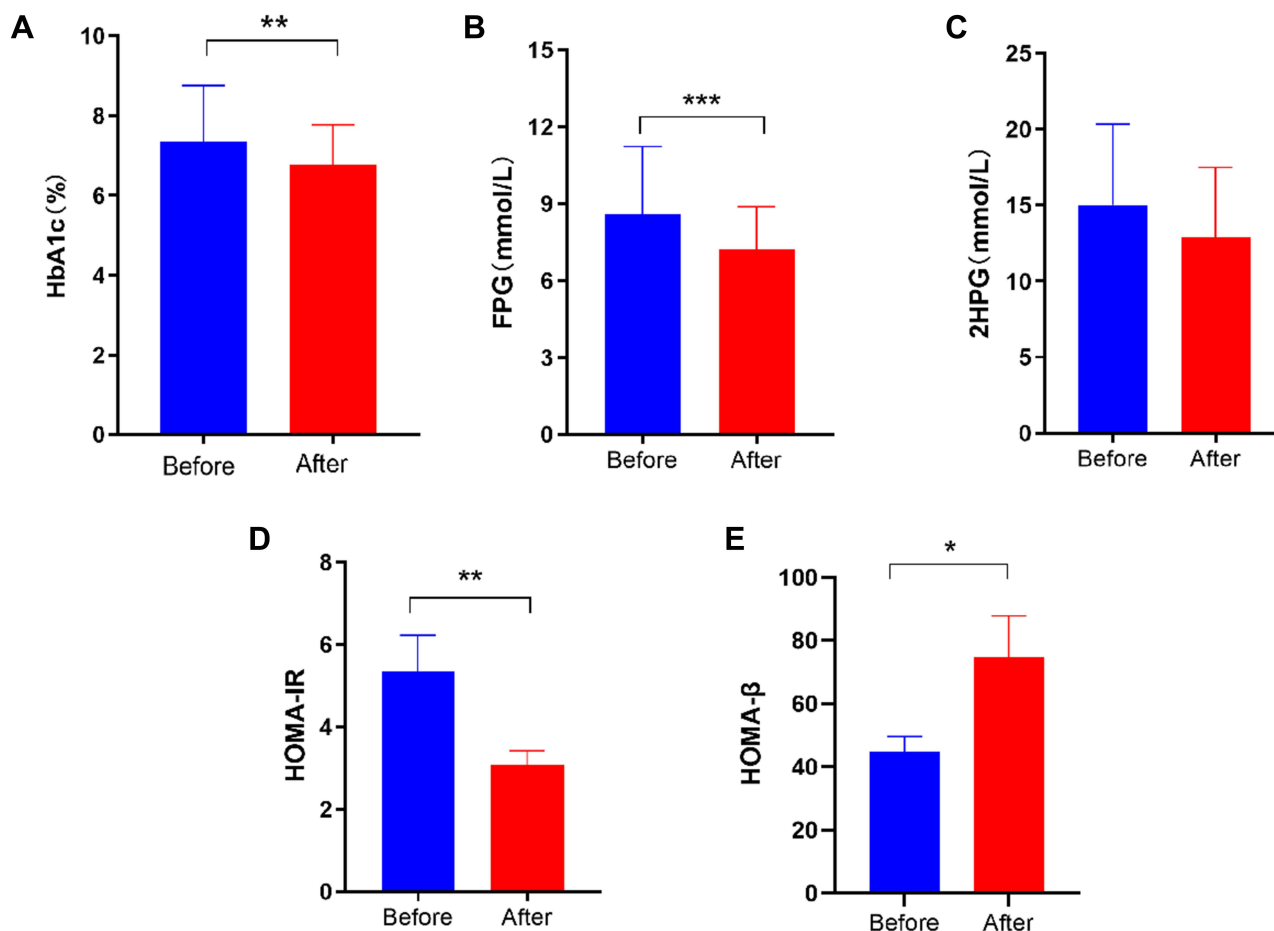
The results of patient evaluations of the hypoglycemic effect of antidiabetic drugs were as follows: 37 patients recognized the hypoglycemic effect of antidiabetic drugs, but stopped taking it due to side effects; 63 patients were afraid to develop side effects; 43 patients believed that the hypoglycemic effect was immediate and experienced no side effects; 4 patients administered antidiabetic drugs co-therapy to lower blood glucose, but the effect was still modest (Figure 2E).

In addition, the questionnaire results showed that 9 patients did not control their diet and exercise well, and 7 patients had poor blood glucose control (Figure 2F).

## Clinical Outcomes

The short-term hypoglycemic effect of the enrolled patients was evaluated by HbA1c, FPG, 2hPG, HOMA-IR, and HOMA- $\beta$  after taking JTSH tablets regularly for 2 months.

Laboratory test results were obtained in 74 patients before and after receiving JTSH tablet for 2 months. As shown in Figure 3A, the mean value of HbA1c at baseline was 7.35%, which decreased to 6.77% after 2 months of treatment ( $P=0.004$ ). After 2 months of treatment with JTSH tablet, the mean value of FPG decreased from 8.60 to 7.19 mmol/L



**Figure 3** Hypoglycemic effect and islet protection effect of Jang Tang San Huang tablets (JTSH tablets) in the treatment of type 2 diabetes mellitus. **(A)** Changes in glycosylated haemoglobin levels before and after treatment with JTSH tablet in 68 patients. **(B)** Changes in 2-hour postprandial blood glucose levels before and after treatment with JTSH tablets in 57 patients. **(C)** Changes in glycosylated haemoglobin levels before and after treatment with JTSH tablet in 43 patients. **(D)** Changes in HOMA-IR levels before and after treatment with JTSH tablet in 37 patients. **(E)** Changes in HOMA-β levels before and after treatment with JTSH tablet in 43 patients. **Notes:** *P*-values are calculated comparing post-treatment with JTSH tablets and the baseline values. \**P* < 0.05; \*\**P* < 0.01; \*\*\**P* < 0.001. **Abbreviations:** 2HPG, 2-hour postprandial blood glucose; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; HOMA-IR, homeostasis model assessment of the insulin resistance index; HOMA-β, homeostasis model assessment of β-cell function.

(*P*=0.000) (Figure 3B); the mean value of 2hPG decreased from 15.03 to 12.89 mmol/L (*P*=0.300) (Figure 3C); the mean values of HOMA-IR decreased from 5.36 to 3.08 (*P*=0.003) (Figure 3D). However, the mean values of HOMA-β after treatment with JTSH tablets increased from 44.73 to 74.82 (*P*=0.041) (Figure 3E). Significant differences were observed in the change in HbA1c, FPG, HOMA-IR, and HOMA-β (*P*<0.050).

## Correlation Analysis

The mean duration of administering the JTSH tablet treatment was  $2.57 \pm 1.45$  years. The effective degree of freedom was 1, which implied the positive correlation between the time of JTSH tablet administration and good glycemic control in patients with T2DM. As shown in Table 4, univariate logistic regression analysis determined that taking JTSH tablets for 1 year can reduce the risk of poor hypoglycemic effect in 18.45% of patients (*P*=0.049). In contrast, poor self-management of diet and exercise was observed to increase the risk of poor hypoglycemic effect by 1.75 times. The multivariate logistic regression model I results showed that taking JTSH tablets for 1 year might reduce the risk of poor hypoglycemic effect by 14.5% (RR=0.855, 95% CI:0.595,1.089, *P*=0.160). The multivariate logistic regression model II results showed that RR was 0.830 (95% CI:0.578, 1.021, *P*=0.066).



**Table 4** Logistic Regression Between JTSH Tablet Administration and Glycaemic Control

	Univariate Logistic Model		Multivariate Logistic Model I		Multivariate logistic Model II	
	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
Age	0.995 (0.962, 1.025)	0.349	0.99454 (0.996, 1.030)	0.758		
Sex	0.587 (0.210, 1.063)	0.064	0.7093 (0.260, 1.528)	0.307		
BMI	0.993 (0.860, 1.086)	0.453	0.9571 (0.838, 1.054)	0.287		
Diet and exercise	2.756 (1.477, 26.598)	0.022*	2.3531 (1.249, 25.269)	0.024*	2.662 (1.285, 24.004)	0.030*
CHM	0.816 (0.574, 0.992)	0.040*	0.855 (0.595, 1.089)	0.160	0.830 (0.578, 1.021)	0.066

Note: \*P < 0.05.

Abbreviations: JTSH tablet, Jiang Tang San Huang tablet; BMI, body mass index; CHM, Chinese herbal medicine; RR, relative risk; CI, confidence interval.

## Discussion

This retrospective study utilized outpatient data obtained and provides an overview of JTSH tablet usage by patients with T2DM in the southern region of China. JTSH Tablets have been used in the clinical setting for more than 20 years, and their effectiveness and safety have been reported in China.<sup>26,31</sup> As early as 1998, JTSH tablet were reported to have a 79% hypoglycemic efficacy rate and improved the main clinical symptoms of T2DM.<sup>26</sup> The longest treatment time of taking JTSH tablets was about 10 years, and no obvious hepatorenal toxicity was found after long-term use. The animal experiments observed that JTSH tablet have no acute, long-term, or delayed toxicity and are safe within the therapeutic dose range.<sup>32</sup>

Animal experiments have shown that JTSH tablet can reduce tumor necrosis factor- $\alpha$ , interleukin-1 $\beta$ , and intercellular adhesion molecule-1 expression to improve inflammatory response of islet  $\beta$  cells in db/db mice,<sup>33</sup> and reduce blood sugar in diabetic rats by stimulating the synthesis of hepatic glycogen and inhibiting its decomposition.<sup>26</sup> Network pharmacology was used to predict that the active ingredients of JSTH tablet were quercetin, kaempferol and isorhamnetin, and the hypoglycemic targets were estrogen receptor, peroxisome proliferator activated receptor  $\gamma$  (PPARG) and epidermal growth factor receptor; The KEGG pathway is enriched in the end products of advanced glycation end products-receptor for AGE pathway.<sup>34</sup>

In this study, we conducted a questionnaire survey to assess the satisfaction achieved among patients receiving long-term treatment with JTSH tablets. We designed this questionnaire inspired the PRO scale for cancer patients treated with JTSH tablets. The preliminary questionnaire was designed to explore the reason, purpose and efficacy satisfaction of the increasing number of patients receiving JTSH tablets treatment. The results of the questionnaire showed that the patients were highly satisfied with the hypoglycemic effect of JTSH tablet. Patients who believed that JTSH tablets had no hypoglycemic effect still affirm its advantages in conditioning the body and improving symptoms. Furthermore, linear regression models demonstrated that each 1-year treatment with JTSH tablets may reduce the risk of poor glycemic control by 17.0%.

Our research findings present not only the short- and long-term clinical efficacy of simple JTSH tablet treatment, but also the perceived efficacy from the patients' perspective, which paves the way for the establishment of a PRO scale for evaluating the therapeutic efficacy of CHM in T2DM patients.

During the telephone follow-up, 25.85% of patients reported discontinuing JTSH tablets because of the new coronary pneumonia epidemic and could not return to hospital regularly to obtain the medicine, indicating that the epidemic had changed the medication mode of patients with T2DM. Fourteen patients could be stopped after maintenance treatment of JTSH tablets to achieve a clinical cure state, and there was no relapse state by regular blood examination follow-up. In addition, we found a strong correlation between a healthy diet and exercise management and good glycemic control.

The study has some limitations. First, the reported results are from a single retrospective clinical study, and the insufficient number of enrolled cases limits the level of evidence. Therefore, additional multicenter prospective clinical trials and animal studies are needed to provide conclusive evidence. Second, in the questionnaire survey and follow-up,

we learned that the symptoms that patients consciously improved most were fatigue, insomnia, poor appetite, constipation, and emotional anxiety among others, but our PROs scale did not describe the extent of symptom improvement in detail.

Our study used a questionnaire to evaluate the efficacy of JTSH tablet and consequently provided a treatment plan for a prospective clinical study. In the future, we will conduct a large-scale questionnaire to develop a PRO for the hypoglycemic efficacy of JTSH tablet and self-management in patients with T2DM and we will conduct a prospective cohort study to confirm the hypoglycemic effect and mechanism of these herbs. This will provide evidence for the combined strategy of JTSH tablets and antidiabetic drugs in treating T2DM.

## Conclusion

Good blood glucose control may be positively correlated with the treatment time of the JTSH tablets. Patients with T2DM are satisfied with the antidiabetic effect of JTSH tablets, which can significantly reduce blood glucose and insulin resistance and improve the function of islet cells.

## Data Sharing Statement

The original data is available upon request by email from (Cui Shao: shaocui2022@sina.com).

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## Author Contributions

All authors made a significant contribution to the work reported in the conception, study design, acquisition of data, analysis; participated in writing, substantially revising or critically reviewing the manuscript. All authors have agreed on any significant changes in all versions of the article before submission. All authors agreed to take responsibility and be accountable for the contents of the manuscript.

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## Disclosure

The authors report no conflicts of interest in this work.

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