Effectiveness and safety of the TRIO optimal health management program in patients with type 2 diabetes mellitus (T2DM): A real-world study of initiating basal insulin therapy

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Chenxi Li[1] Dr med; Lixin Guo[2] MEd; Lixin Shi[3] MEd; Li Chen[4] MEd; Liming Chen[5] MEd; Yaoming Xue[6] MEd; Hong Li[7] MEd; Yuzhen Liang[8] MEd; Jing Yang[9] MEd; Weimin Wang[1] MEd; Dalong Zhu[1] MEd

[1]Department of Endocrinology, Endocrine and Metabolic Disease Medical Center Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School Nanjing CN
[2]Department of Endocrinology Graduate School of Peking Union Medical College, Chinese Academy of Medical Sciences Beijing CN
[3]Department of Endocrinology ,Affiliated Hospital of Guiyang Medical University Guiyang CN
[4]Department of Endocrinology Qilu Hospital of Shandong University Jinan CN
[5]NHC Key Laboratory of Hormones and Development, Tianjin Key Laboratory of Metabolic Diseases, Chu Hsien-I Memorial Hospital & Tianjin Institute of Endocrinology Tianjin Medical University Tianjin CN
[6]Department of Endocrinology & Metabolism, Nanfang Hospital Southern Medical University Guangzhou CN
[7]Department of Endocrinology and Metabolism, The First Affiliated Hospital of Kunming Medical Universit Kunming CN
[8]Department of Endocrinology The Second Affiliated Hospital of Guangxi Medical University Nanjing CN
[9]Department of Endocrinology, First Hospital of Shanxi Medical University Shanxi Medical University Taiyuan CN

Corresponding Author:
Dalong Zhu MEd
Department of Endocrinology, Endocrine and Metabolic Disease Medical Center
Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School
No.321 Zhongshan Road
Nanjing
CN

Abstract

Background: Diabetes, a chronic disease necessitating long-term treatment and self-management, presents significant challenges for patients who spend most of their treatment time outside of hospitals. The potential of digital therapeutics for diabetes has garnered recognition from different organizations. Although some prior studies have demonstrated successful reductions in patients' blood glucose levels and body weight through digital diabetes programs, many studies were limited by including prediabetes patients, patients treated with mostly premixed insulin or evaluating user engagement outcomes rather than clinical outcomes. Consequently, limited evidence remains regarding the effectiveness of health management mobile applications specifically designed for T2DM patients initiating BI (basal insulin).

Objective: This prospective observational study evaluated the effectiveness and safety of the TRIO optimal health management program for patients with type 2 diabetes mellitus (T2DM) initiating basal insulin therapy in a real-world setting.

Methods: Patients aged 18 to 85 years with inadequate glycemic control (baseline HbA1c ?7.0%) starting basal insulin therapy were enrolled from outpatient and inpatient. The study duration was 3 months, with health education and phone-based follow-up assessments. Data collected included patient characteristics, medical history, baseline diabetes conditions, treatment compliance, glycemic control, and safety indicators.

Results: A total of 199,431 patients were included and 118,134 patients completed the 3-month follow-up. The mean baseline HbA1c was 9.2%, the mean duration of diabetes was 7.3 years, and 80.4% of patients were using basal insulin with oral antihyperglycemic drugs. After the intervention, mean HbA1c decreased by -2.59% from baseline, with 55.6% achieving the target HbA1c level of <7.0%. Patients who set a lower fasting plasma glucose (FPG) goals (<6.1 mmol/L) showed greater HbA1c reductions and higher target achievement compared to those with FPG goal ?6.1 mmol/L. Factors such as complications, diabetes duration, and baseline HbA1c levels influenced the magnitude of HbA1c reduction. The presence of complications, shorter diabetes duration, higher baseline HbA1c was significantly associated with increased hypoglycemia incidence risk.

Conclusions: The TRIO optimal health management program effectively improved glycemic control in patients with T2DM

initiating basal insulin therapy. Individualized treatment approaches considering patient characteristics and glycemic goals are vital for optimal outcomes. Clinical Trial: This is a real-world study of initiating basal insulin therapy.

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1 Department of Endocrinology, Endocrine and Metabolic Disease Medical Center, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, China.

2 Branch of National Clinical Research Centre for Metabolic Diseases, Nanjing, China.

3 Department of Endocrinology, Graduate School of Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China

4 Department of Endocrinology, Affiliated Hospital of Guiyang Medical University, Guiyang, China.

5 Department of Endocrinology, Qilu Hospital of Shandong University, Jinan, China.

6 NHC Key Laboratory of Hormones and Development, Tianjin Key Laboratory of Metabolic Diseases, Chu Hsien-I Memorial Hospital & Tianjin Institute of Endocrinology, Tianjin Medical University, Tianjin, China.

7 Department of Endocrinology & Metabolism, Nanfang Hospital, Southern Medical University, Guangzhou, China.

8 Department of Endocrinology and Metabolism, The First Affiliated Hospital of Kunming Medical University, Kunming, China.

9 Department of Endocrinology, The Second Affiliated Hospital of Guangxi Medical University, Nanning, China.

10 Department of Endocrinology, First Hospital of Shanxi Medical University, Shanxi Medical University, Taiyuan, Shanxi, China.

Running Head: The TRIO program in T2DM patients: A real-world study

*Correspondence

Weimin Wang, Department of Endocrinology, Nanjing Drum Tower Hospital, Affiliated Hospital of

Medical School, Nanjing University, No. 321 Zhongshan Road, Nanjing, 210008, China.

Email: wwmlyg@189.cn

Dalong Zhu, Department of Endocrinology, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, No. 321 Zhongshan Road, Nanjing, 210008, China.

Email: zhudalong@nju.edu.cn

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control, and safety indicators.

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Conclusions:

The TRIO optimal health management program effectively improved glycemic control in patients with T2DM initiating basal insulin therapy. Individualized treatment approaches considering patient characteristics and glycemic goals are vital for optimal outcomes.

Keywords:

type 2 diabetes; TRIO optimal health management program; initiating basal insulin therapy; glycemic control; real-world study

Introduction

Background

The prevalence of type 2 diabetes mellitus (T2DM) in China is experiencing a rapid surge due to lifestyle changes and an aging population. As per the 2018 ADA criteria, the estimated prevalence of total diabetes and prediabetes among Chinese adults escalated to 12.8% and 35.2%, respectively, between 2015 and 2017 (1). Despite the wide range of medication options available for antidiabetic

treatment, glycemic control rates among patients with T2DM remain suboptimal (2). A national survey conducted in 2018 revealed that only 32.9% of diabetic patients received treatment, with only half of them (50.1%) achieving adequate glycemic control (3).

Diabetes, a chronic disease necessitating long-term treatment and self-management, presents significant challenges for patients who spend most of their treatment time outside of hospitals (4). When lifestyle intervention and oral antidiabetic drugs (OADs) fail to provide optimal control, patients with type 2 diabetes are required to initiate injectable therapies, mostly basal insulin, according to 2020 Chinese guidelines for T2DM management (5).

Previous randomized controlled trials (RCTs) and observational studies have shown the efficacy of BI in controlled trials (6) and real-world settings (7). Maintaining a delicate equilibrium between achieving optimal blood glucose control and mitigating hypoglycemia risks is a pivotal concern. This involves not only the appropriate titration of insulin but also diligent self-monitoring of blood glucose levels, both of which are integral to sustaining effective glycemic management. Consequently, establishing an optimal diabetes management framework encompassing health education, consistent professional follow-up, and comprehensive self-monitoring tools becomes imperative for effectively managing type 2 diabetes patients. (8). The lack of comprehensive and patient-centered approaches in current healthcare systems further compounds the burden of diabetes management. Time constraints and resource availability often limit traditional health education and face-to-face interactions with healthcare providers. As a result, there is a growing need for innovative solutions to bridge these gaps and provide ongoing support to individuals with type 2 diabetes (9–11). The emergence of digital tools such as mobile applications and WeChat mini-programs has increased application in diverse therapeutic domains, such as attention deficit hyperactivity disorder, cancer, asthma, and insomnia tools to augment patient self-management (12).

Objective

The potential of digital therapeutics for diabetes has garnered recognition from different organizations such as the Centers for Disease Control and Prevention (CDC) and the Digital

Therapeutics Alliance (DTA) (13). Although some prior studies have demonstrated successful reductions in patients' blood glucose levels and body weight through digital diabetes programs up to an HbA1c reduction of 0.49% (14), many studies were limited by including prediabetes patients (15), patients treated with mostly premixed insulin (16) or evaluating user engagement outcomes rather than clinical outcomes (17). Consequently, limited evidence remains regarding the effectiveness of health management mobile applications specifically designed for T2DM patients initiating BI.

Our study aims to assess the effectiveness and safety of TRIO, a personalized health management program that integrates patients, nurses, and physicians. Unlike conventional acronyms or abbreviations, TRIO does not represent a longer phrase but it is rather representative of the three important pillars in the comprehensive diabetes management: physician, nurse, and patient. This program combines traditional health education with a mobile application to enhance diabetes management. Through this evaluation, we aspire to contribute to the understanding of effective approaches in optimizing glycemic control and promoting patient well-being.

Methods

Study Design and Population

This prospective, 3-month observational program aimed to evaluate the effectiveness and safety of TRIO, an optimal health management program for patients with T2DM initiating BI therapy in a real-world setting. Participants were recruited from outpatient and at the time of discharge from inpatient departments between Dec 1, 2019, and Dec 31, 2021, involving 594 hospitals in China. Patients were assessed for their suitability by the following criteria: 1) aged between 18 and 85 years old; 2) T2DM patients who were inadequately controlled by OADs at the time of enrollment (i.e., baseline HbA1c level ≥7.0%); 3) initiating BI therapy during the program period, meaning they had not used BI within 12 weeks prior to enrollment; 4) absence of mental disorders or communication

impairments; 5) absence of severe illnesses or limitations regarding follow-up. Patients who fulfilled these eligibility requirements were enrolled upon their willingness and provided informed consent. On the first day of enrollment, patients received health education from nurses, and physicians determined the Fasting Plasma Glucose (FPG) targets for the patients. Patients were also asked to follow the WeChat official account of the TRIO program, through which knowledge about diabetes management would be sent. Follow-up assessments were conducted via phone calls at 1, 2, 4, 8, and 12 weeks. The frequency and follow-up methods were tailored to each patient's FPG level. If the FPG was less than 7 mmol/L, a phone call was not scheduled for the next follow-up visit, and only a WeChat message was sent.

Ethics Approval

The protocol received approval from the Institutional Review Board (IRB) of each participating hospital, and all patients provided written informed consent following the principles of the Helsinki Declaration. All patients were informed that their participation was voluntary, that they could withdraw from the study at any time without stating reasons, and that non participation and withdrawal would not result in any disadvantage to them.

Data Collection

Baseline information was collected by interviews at the hospital enrollment, including demographics, disease characteristics, medical history, physical examination, BI types, starting dosage and concomitant antidiabetic drugs (bolus insulin, GLP-1 RA or OAD) used with BI. Laboratory tests including HbA1c and FPG were obtained in hospitals at baseline, while glycemic control regarding HbA1c and self-monitoring blood glucose (SMBG) including fasting blood glucose (FBG), dosage and hypoglycemia information during follow-up time were self-reported. Self-reported data were collected through phone calls by nurses or uploaded via a smart blood glucose device or input into the TRIO WeChat official account by the patients.

Outcomes

Primary Effectiveness Endpoints:

The primary effectiveness endpoint of our analysis is the change in HbA1c levels from baseline to month 3.

Secondary Effectiveness Endpoints:

In addition to the primary endpoint, we also examined various other measures related to glycemic control. These secondary endpoints include changes in FBG levels from baseline to month 3, the achievement of target HbA1c levels (<7%), the achievement of target FBG levels (<7, <6.1 mmol/L), and an assessment of changes in basal insulin dose.

Safety Endpoints:

Our safety endpoints include monitoring and assessing the incidence and rates of hypoglycemia events and the evaluation of composite endpoints. It included incidence and rates of hypoglycemia events during the 3 months as well as a composite endpoint that encompassed percentage of patients reaching target HbA1c and FBG levels without experiencing hypoglycemia events.

Statistical Methods

Continuous variables were described using mean, and standard deviation, while categorical variables were presented as frequencies and percentages. For continuous effectiveness indicators, paired t-test was applied to test significance of change from baseline to month 3 in HbA1c or FPG in the total population. Analysis of Covariance (ANCOVA) was used to compare these changes between subgroups, including patient source (inpatient/outpatient), complication status (no/yes), duration of diabetes (< 5 years/≥5 years), baseline HbA1c (7-8%/8-9%/9-10%/≥10%), and FBG goal setting (≥6.1 mmol/L/<6.1 mmol/L). Least square (LS) mean (standard error [SE]) and LS mean difference were provided with 95% confidence intervals (CI). For binary effectiveness outcomes (HbA1c<7%, FBG <7 mmol/L or FBG <6.1 mmol/L), multivariable logistic regression models were applied to

explore the association of subgroups with outcomes and variables included in the model were the same as ANCOVA model. Hypoglycemic incidence and rate were evaluated by self-monitoring blood glucose (SMBG) uploaded by the smart glucose blood device or manual input to the TRIO platform by patients. Hypoglycemic incidence (percentage of patients with SMBG ≤3.9 mmol/L or SMBG <3.0 mmol/L) was analyzed using logistic regression and odds ratio (OR) with CI (OR, 95%) were used as the effect size; hypoglycemic rate (numbers of events per patient-year) was investigated by Poisson regression and risk ratio (RR) with CI (RR, 95%) were used as the effect size for this analysis. Composite endpoints including HbA1c <7% without SMBG ≤3.9 mmol/L, FBG <7 mmol/L without SMBG ≤3.9 mmol/L, and FBG <6.1 mmol/L without SMBG ≤3.9 mmol/L were also explored using Logistic regression. All the analyses were conducted using SAS 9.4 (SAS Institute, Inc, Cary, NC), and a 2-sided *P*-value<0.05 was considered statistically significant.

Results

Participant Recruitment

Between Dec 1, 2019, and Dec 31, 2021, a total of 225,764 patients were recruited from 594 hospitals. 26,333 patients were excluded because of violating inclusion or meeting exclusion criteria, leaving 199,431 patients remained at baseline. Among them, 81,297 patients were lost to follow-up within the first three months, resulting in 118,134 patients who completed the 3-month follow-up with measurements of either HbA1c or FPG (Figure 1).

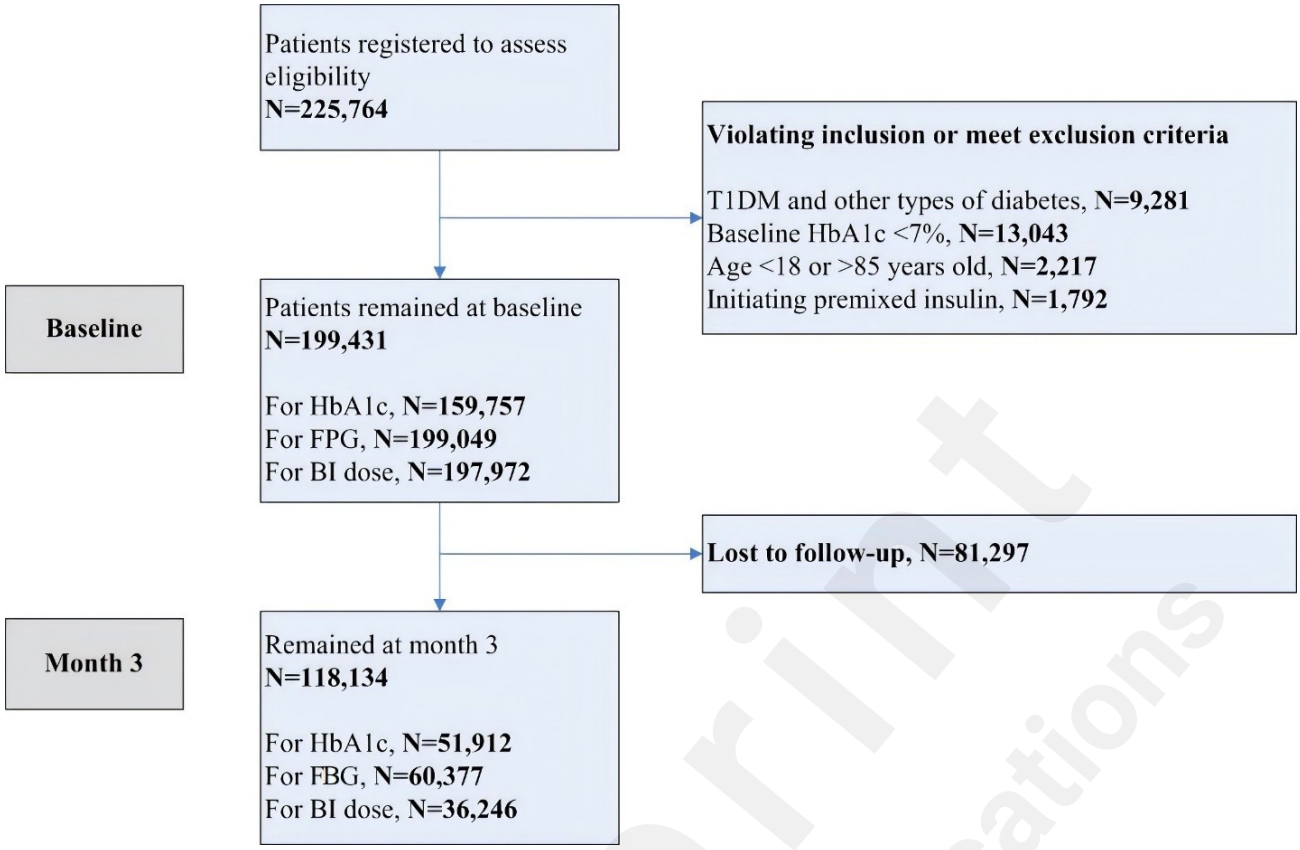

Figure 1. Flowchart of participating patient enrollment

Baseline Characteristics

The mean (SD) age of the patients at baseline was 57.3 (12.5) years, with 42.8% of participants being women. The average body mass index (BMI) was 24.8 kg/m². At baseline, the mean HbA1c, FPG, and PPG levels were 9.6%, 9.5 mmol/L, and 12.7 mmol/L, respectively. The mean duration of diabetes was 7.3 years. The most common complications or comorbidities observed in our patient cohort were hypertension (28.4%), hyperlipidemia (16.4%), and peripheral neuropathy (32.2%). Most patients were taking basal insulin with oral antihyperglycemic drugs (80.4%), with some also using prandial insulin concurrently.

Outpatients had a slightly higher mean age of 57.7 (SD 12.2) years compared to inpatients with a mean age of 57.0 (SD 12.6) years. Gender distribution revealed that 56.3% of outpatients were male, while 57.6% of inpatients were male. Moreover, the duration of diabetes was slightly longer in inpatients, with a mean of 7.4 years (SD 6.8) compared to outpatients with 7.0 years (SD 6.3). Both groups displayed a similar average BMI of 24.8 kg/m² and exhibited comparable values for blood pressure, lipid levels such as triglycerides, total cholesterol, LDL, and baseline HbA1c. While baseline FPG (10.3 vs. 9.0 mmol/L) and PPG (14.0 vs. 12.2

mmol/L) were slightly higher in outpatients than inpatients. A notable difference was observed in the percentage of patients with complications or comorbidities, with 31.3% of inpatients having hypertension compared to 22.9% of outpatients, and 38.1% of inpatients having peripheral neuropathy compared to 21.3% of outpatients. Inpatients also had a higher proportion of patients being treated with BI in combination with prandial insulin, accounting for 20.3% of inpatients as opposed to 15.5% of outpatient (Table 1).

No clinically significant differences in baseline characteristics were observed between patients who remained in the study at month 3 and those who were lost to follow-up.

Table 1 Baseline characteristics of patients

Baseline characteristics	Outpatient (*N*=70,786)	Inpatient (*N*=128,645)	All (*N*=199,431)
Age (years)	57.7 (12.2)	57.0 (12.6)	57.3 (12.5)
Gender			
Male	39802 (56.3)	74064 (57.6)	113866 (57.2)
Female	30902 (43.7)	54435 (42.4)	85337 (42.8)
BMI (kg/m^2)	24.8 (3.3)	24.8 (3.5)	24.8 (3.5)
Duration of diabetes (years)	7.0 (6.3)	7.4 (6.8)	7.3 (6.6)
SBP (mmHg)	131.8 (15.4)	131.8 (16.5)	131.8 (16.2)
DBP (mmHg)	79.9 (10.1)	79.6 (10.4)	79.7 (10.3)
Triglycerides (mmol/L)	2.3 (2.0)	2.3 (2.1)	2.3 (2.1)
Total cholesterol (mmol/L)	4.6 (1.5)	4.7 (1.5)	4.7 (1.5)
LDL (mmol/L)	2.8 (1.1)	2.8 (1.1)	2.8 (1.1)
BI dose (U/day)	15.2 (5.5)	16.2 (6.1)	15.9 (5.9)
BI dose (U/kg/day)	0.23 (0.08)	0.24 (0.09)	0.24 (0.09)
eGFR (ml/min/1.73m^2)			
<90	953 (23.6)	3999 (22.0)	4952 (22.3)
[90,120)	1135 (28.2)	4738 (26.1)	5873 (26.5)
≥120	1942 (48.2)	9424 (51.9)	11366 (51.2)
Baseline HbA1c (%)	9.3 (1.8)	9.7 (2.1)	9.6 (2.0)
Baseline FPG (mmol/L)	10.3 (3.3)	9.0 (3.2)	9.5 (3.3)
Baseline PPG (mmol/L)	14.0 (4.4)	12.2 (4.0)	12.7 (4.2)
Regimen			
BI alone ± OAD	59176 (83.8)	100754 (78.5)	159930 (80.4)
BI + prandial insulin ± OAD	10924 (15.5)	26037 (20.3)	36961 (18.6)
BI + GLP-1 RA ± OAD	527 (0.7)	1551 (1.2)	2078 (1.0)
Comorbidity			
Hypertension	15687 (22.9)	39950 (31.3)	55637 (28.4)
Hyperlipemia	8992 (13.1)	23248 (18.2)	32240 (16.4)
Left ventricular hypertrophy	53 (0.08)	149 (0.12)	202 (0.10)
Atrial fibrillation	80 (0.12)	213 (0.17)	293 (0.15)
Complication			
Stroke	1409 (2.1)	4511 (3.5)	5920 (3.0)
Coronary heart disease	4601 (6.7)	11656 (9.1)	16527 (8.3)
Diabetic nephropathy	3266 (4.8)	11209 (8.8)	14475 (7.4)
Diabetic retinopathy	6058 (8.9)	17329 (13.6)	23387 (11.9)
Diabetic foot	663 (1.0)	3253 (2.6)	3916 (2.0)
Peripheral neuropathy	14565 (21.3)	48580 (38.1)	63145 (32.2)
Lower extremity angiopathy	2844 (4.2)	10601 (8.3)	13445 (6.9)

Initial Regimens and Adherence to BI Treatment

During the intervention, the majority of patients initiated insulin glargine (89.1%) as their primary treatment, while a smaller proportion started with insulin determir (3.3%), NPH insulin (0.4%), or insulin degludec (4.5%). Alongside basal insulin treatment, 41.0%, 28.2%, and 9.7% of patients were concurrently taking 1, 2, and ≥3 oral antihyperglycemic drugs (OADs), respectively. The most commonly used OADs were metformin (49.4%) and α-glucosidase inhibitors (33.6%), followed by SGLT2 inhibitors (16.4%), DPP-4 inhibitors (14.8%), sulfonylureas (5.2%), glinides (4.5%), and thiazolidinediones (3.9%). Sulfonylureas were more frequently prescribed to outpatients (7.3%) than inpatients (4.1%), while SGLT-2 inhibitors were more commonly used in inpatients (18.2%) than outpatients (12.9%).

Glycemic Outcomes

At the end of the 3-month management intervention period, the mean HbA1c level among 44,847 participants with eligible self-reported mean (SD) HbA1c measurements was 6.89% (0.90). This represented a mean decrease (SE) in HbA1c by -2.59% (0.01) ($P < 0.001$) from baseline (Table 2). Regarding FBG levels, at the end of month 3, the mean FBG level among 60,365 participants with eligible self-reported FBG measurements was 6.81 (1.4) mmol/L, indicating an average decrease in FBG by -2.77 (0.01) mmol/L ($P <0.001$) from baseline (Table 2, Figure S1). For the HbA1c target, 28,858 participants (55.6%) achieved the target HbA1c level of <7.0% after the three-month intervention period (Table 3). Similarly, 37,017 (61.3%) and 17,633 (29.2%) participants reached FBG levels <7. 0 and <6.1 mmol/L, respectively at the end of the 3-month intervention period.

In the subgroup analyses, patients with complications experienced a slightly less decrease in HbA1c (LS Mean difference: 0.07, 95% CI 0.05 – 0.09) compared to those without. Considering the duration of diabetes, patients with a duration of 5 years or more exhibited a smaller decrease in HbA1c (LS Mean difference: 0.09, 95% CI 0.07 – 0.11) compared to those with a duration <5 years. Higher

baseline HbA1c level was also associated with a greater reduction. Compared with patients with baseline HbA1c 7-8%, patients with a baseline HbA1c in the range of 8-9 % had the smallest decrease (LS Mean difference: -0.83, 95% CI -0.86 – -0.79), while patients with a baseline HbA1c of 10% or higher had the largest decrease (LS Mean difference: -4.04, 95% CI -4.08 – -4.00). Also, patients with initial FBG goal setting <6.1 mmol/L had a greater decrease in their HbA1c (LS Mean difference: -0.36, 95% CI –0.38 – -0.34) compared to FBG goal ≥6.1 mmol/L (Table 2). In the subgroup analysis exploring factors related to FBG reduction, consistent results with HbA1c reductions were found that greater reductions were seen in patients with no complications, diabetes duration <5 years, and an initial FBG goal setting <6.1 mmol/L, except for baseline HbA1c. Patients with lower baseline HbA1c exhibited higher reductions in FBG from baseline. (Table 2).

Table 2 HbA1c and FBG change from baseline to month 3 after initiation of basal insulin therapy with TRIO monitoring

	N	Baseline	Month 3	LS Mean (SE)	*P*-value	LS Mean diff. (95% CI)	*P*-value
HbA1c change from baseline to month 3							
All	44847	9.48 (1.98)	6.89 (0.90)	-2.59 (0.01) [a]	<0.001		
Patient sources							
Outpatient	14893	9.10 (1.71)	6.93 (0.81)	-2.63 (0.02)	<0.001	Reference	
Inpatient	29954	9.67 (2.07)	6.88 (0.95)	-2.71 (0.01)	<0.001	-0.08 (-0.1, -0.06)	<0.001
Complication							
No	17963	9.33 (1.89)	6.83 (0.85)	-2.71 (0.02)	<0.001	Reference	
Yes	20389	9.58 (2.01)	6.96 (0.93)	-2.64 (0.01)	<0.001	0.07 (0.05, 0.09)	<0.001
Duration, years							
<5	18950	9.69 (2.14)	6.80 (0.88)	-2.72 (0.02)	<0.001	Reference	
≥5	25888	9.32 (1.83)	6.96 (0.92)	-2.63 (0.01)	<0.001	0.09 (0.07, 0.11)	<0.001
Baseline HbA1c, %							
7-8	9250	7.42 (0.33)	6.78 (0.88)	-0.79 (0.02)	<0.001	Reference	
8-9	12485	8.34 (0.32)	6.86 (0.89)	-1.62 (0.02)	<0.001	-0.83 (-0.86, -0.79)	<0.001
9-10	8342	9.35 (0.31)	6.94 (0.86)	-2.54 (0.01)	<0.001	-1.75 (-1.79, -1.70)	<0.001
≥10	14770	11.81 (1.57)	6.97 (0.95)	-4.83 (0.02)	<0.001	-4.04 (-4.08, -4.00)	<0.001
FBG goal setting,							

mmol/L							
≥6.1	36935	9.54 (1.98)	6.96 (0.87)	-2.49 (0.01)	<0.001	Reference	
<6.1	7904	9.22 (1.96)	6.58 (0.99)	-2.85 (0.02)	<0.001	-0.36 (-0.38, -0.34)	<0.001
FBG change from baseline to month 3							
All	60365	9.58 (3.30)	6.81 (1.40)	-2.77 (0.01[a])	<0.001		
Patient sources							
Outpatient	21055	10.35 (3.27)	6.86 (1.39)	-2.61 (0.02)	<0.001	Reference	
Inpatient	39310	9.17 (3.25)	6.79 (1.41)	-2.68 (0.02)	<0.001	-0.07 (-0.09, -0.04)	<0.001
Complication							
No	22927	9.86 (3.16)	6.68 (1.32)	-2.71 (0.02)	<0.001	Reference	
Yes	28252	9.14 (3.17)	6.94 (1.45)	-2.58 (0.02)	<0.001	0.13 (0.11, 0.16)	<0.001
Duration, years							
<5	24683	9.74 (3.54)	6.57 (1.27)	-2.78 (0.02)	<0.001	Reference	
≥5	35666	9.48 (3.13)	6.98 (1.46)	-2.50 (0.02)	<0.001	0.28 (0.25, 0.3)	<0.001
Baseline HbA1c, %							
7-8	10005	8.35 (2.13)	6.68 (1.26)	-2.75 (0.02)	<0.001	Reference	
8-9	13472	9.21 (2.48)	6.79 (1.29)	-2.66 (0.02)	<0.001	0.08 (0.05, 0.12)	<0.001
9-10	9506	9.59 (2.99)	6.85 (1.39)	-2.61 (0.02)	<0.001	0.13 (0.09, 0.17)	<0.001
≥10	18879	10.32 (4.11)	6.83 (1.49)	-2.58 (0.01)	<0.001	0.16 (0.13, 0.20)	<0.001
FBG goal setting, mmol/L							
≥6.1	50482	9.68 (3.32)	6.87 (1.40)	-2.52 (0.02)	<0.001	Reference	
<6.1	9854	9.10 (3.18)	6.53 (1.35)	-2.76 (0.02)	<0.001	-0.24 (-0.28, -0.21)	<0.001

[a] Mean difference (SE) was obtained from the paired t-test in all population.

Regarding target HbA1c <7% at month 3, patients enrolled from inpatient showed a slight advantage over outpatient(OR = 1.16, 95% CI: 1.11 – 1.21, $P < 0.001$), and patients with complications had lower odds of achieving HbA1c target than those without complications (OR = 0.85, 95% CI: 0.81 – 0.89, $P < 0.001$). Those with ≥5 years diabetes duration had lower success rates than those with <5 years (OR = 0.83, 95% CI: 0.79 – 0.87, $P < 0.001$). Lower baseline HbA1c levels were associated with better outcomes. Moreover, to set a FBG target goal levels <6.1 mmol/L at the beginning of the treatment demonstrated higher possibility of reaching HbA1c target <7% at month 3 (OR = 1.8,

95% CI: 1.7 – 1.9, $P < 0.001$) (Table 3). Regarding the FBG target <7 and <6.1 mmol/L at month 3, patients exhibited consistent results as in target HbA1c <7%. Inpatients, patients without complications, patients with diabetes duration less than 5 years, lower HbA1c target, and initial FBG goal setting <6.1 mmol/L were associated with higher odds of achieving the target(Table 3).

Table 3 Target HbA1c and FBG at month 3 after initiation of basal insulin therapy with TRIO monitoring

	N	Month 3	OR (95% CI)	*P*-value
HbA1c <7% at month 3				
All	51912	28858 (55.6)		
Patient sources				
Outpatient	18753	10024 (53.5)	Reference	
Inpatient	33159	18834 (56.8)	1.16 (1.11, 1.21)	<0.001
Complication				
No	20881	12433 (59.5)	Reference	
Yes	23008	12016 (52.2)	0.85 (0.81, 0.89)	<0.001
Duration, years				
<5	21873	13388 (61.2)	Reference	
≥5	30030	15466 (51.5)	0.83 (0.79, 0.87)	<0.001
Baseline HbA1c, %				
7-8	9250	5573 (60.2)	Reference	
8-9	12485	6974 (55.9)	0.85 (0.8, 0.9)	<0.001
9-10	8342	4455 (53.4)	0.77 (0.72, 0.83)	<0.001
≥10	14770	8009 (54.2)	0.72 (0.68, 0.77)	<0.001
FBG goal setting, mmol/L				
≥6.1	43051	22857 (53.1)	Reference	
<6.1	8845	5993 (67.8)	1.8 (1.7, 1.9)	<0.001
FBG <7 mmol/L at month 3				
All	60377	37017 (61.31)		
Patient sources				
Outpatient	21065	12403 (58.9)	Reference	
Inpatient	39312	24614 (62.6)	1.17 (1.12, 1.22)	<0.001
Complication				
No	22936	14952 (65.2)	Reference	
Yes	28254	16239 (57.5)	0.84 (0.8, 0.88)	<0.001
Duration, years				

<5	24686	17053 (69.1)	Reference	
≥5	35675	19955 (55.9)	0.70 (0.67, 0.73)	<0.001
Baseline HbA1c, %				
7-8	10006	6607 (66.0)	Reference	
8-9	13473	8288 (61.5)	0.84 (0.79, 0.89)	<0.001
9-10	9509	5710 (60.0)	0.79 (0.74, 0.85)	<0.001
≥10	18881	11632 (61.6)	0.77 (0.73, 0.82)	<0.001
FBG goal setting, mmol/L				
≥6.1	50493	30112 (59.6)	Reference	
<6.1	9855	6886 (69.9)	1.42 (1.34, 1.5)	<0.001
FBG <6.1 mmol/L at month 3				
All	60377	17633 (29.2)		
Patient sources				
Outpatient	21065	5763 (27.4)	Reference	
Inpatient	39312	11870 (30.2)	1.16 (1.1, 1.22)	<0.001
Complication				
No	22936	7542 (32.9)	Reference	
Yes	28254	7087 (25.1)	0.83 (0.79, 0.87)	<0.001
Duration, years				
<5	24686	8973 (36.3)	Reference	
≥5	35675	8656 (24.3)	0.7 (0.66, 0.73)	<0.001
Baseline HbA1c, %				
7-8	10006	3167 (31.7)	Reference	
8-9	13473	3764 (27.9)	0.84 (0.79, 0.9)	<0.001
9-10	9509	2625 (27.6)	0.87 (0.81, 0.93)	<0.001
≥10	18881	5746 (30.4)	0.91 (0.85, 0.96)	0.002
FBG goal setting, mmol/L				
≥6.1	50493	13538 (26.8)	Reference	
<6.1	9855	4084 (41.4)	1.7 (1.62, 1.8)	<0.001

Insulin dose and satisfaction

Total insulin dose (U/day/kg) change was -0.01 (0.06), from baseline 0.23 (0.09) to month 3 0.22 (0.09) (Table 4). Patients recruited from inpatient, with complications, having diabetes duration ≥ 5

years, with FBG goal setting <6.1 mmol/L and higher baseline HbA1c had a higher starting dose of BI. Among 36,307 patients with both baseline and 3-month basal insulin dosages, 2546 (7.0%) remained unchanged, and 18047 (49.7%) lowered the dosage per kilogram (Table 4). Possible reasons for lack of titration, such as patients reaching FBG targets or experiencing hypoglycemic events, were explored in Table S3. Patients with stable or decreasing dosage during the 3 months had higher starting dose, higher percentages of FBG <7 mmol/L and hypoglycemic incidence at Week 1, 2, 4, 8, and 12 compared to patients with increasing dosage. Patient satisfaction level for TRIO was stable during the study. 99.6% of the patients felt satisfactory or very satisfactory at month 3, and only 0.4% of the patients chose average or below.

Table 4 Basal insulin dose (U/kg) change (SD) from baseline to month 3 by patient sources, with or without complication, duration, baseline HbA1c levels and target FPG levels

	N	Baseline	Month 3	Change
All	36307	0.23 (0.09)	0.22 (0.09)	-0.01 (0.06)
Patient sources				
Outpatient	12999	0.22 (0.08)	0.22 (0.08)	0.00 (0.05)
Inpatient	23038	0.24 (0.09)	0.23 (0.09)	-0.01 (0.06)
Complication				
No	17903	0.23 (0.08)	0.22 (0.08)	-0.01 (0.06)
Yes	17163	0.24 (0.09)	0.23 (0.09)	-0.01 (0.06)
Duration, years				
<5	13993	0.22 (0.08)	0.21 (0.09)	-0.01 (0.06)
≥5	22034	0.24 (0.09)	0.23 (0.09)	0.00 (0.05)
Baseline HbA1c, %				
7-8	5783	0.22 (0.08)	0.22 (0.08)	0.00 (0.05)
8-9	8157	0.23 (0.09)	0.23 (0.09)	-0.01 (0.05)
9-10	5711	0.23 (0.09)	0.22 (0.09)	-0.01 (0.05)
≥10	11003	0.24 (0.09)	0.23 (0.09)	-0.02 (0.06)
FBG goal setting, mmol/L				
≥6.1	30034	0.23 (0.09)	0.22 (0.09)	-0.01 (0.06)
<6.1	5992	0.24 (0.09)	0.23 (0.09)	-0.01 (0.06)
Dose adjustment				
Up	15444	0.22 (0.08)	0.24 (0.08)	0.02 (0.04)
Keep	2546	0.23 (0.08)	0.23 (0.08)	0.00 (0.00)
Down	18047	0.25 (0.09)	0.21 (0.09)	-0.04 (0.06)

Incidence and event rate of Hypoglycemia

Hypoglycemia incidence (≤3.9 mmol/L) in all patients was 27.1% (n = 12,227). Inpatients had a higher incidence compared to outpatients (OR = 1.24, 95% CI: 1.07 – 1.45, *P* = 0.005). Patients with complications experienced more hypoglycemia (OR = 1.25, 95% CI: 1.07 – 1.45), *P* = 0.005).

Longer diabetes duration (≥5 years) was associated with lower hypoglycemia incidence (OR = 0.60, 95% CI: 0.52 – 0.69), *P* < 0.001) (Table 5). Higher baseline HbA1c levels correlated with increased hypoglycemia risk. HbA1c ≥10% had the highest incidence (OR = 1.47, 95% CI: 1.23 – 1.76, *P* < 0.0001) (Table 5). For hypoglycemic events defined by SMBG levels ≤3.9 mmol/L, a total of 7,619 events occurred, yielding an event rate of 2.49 events per person-year (Table 6). Notable trends included higher hypoglycemia rates for inpatient sources compared to outpatient sources (RR = 1.25, 95% CI: 1.08 – 1.46, *P* = 0.004), higher rates in patients with complications compared to those without (RR = 1.25, 95% CI: 1.07 – 1.47, *P* = 0.006), and a lower rate in patients with a diabetes duration ≥5 years (RR = 0.67, 95% CI: 0.59 – 0.77, *P* < 0.001). Additionally, elevated baseline HbA1c levels (≥10%) were associated with a higher hypoglycemia rate (RR = 1.37, 95% CI: 1.15 – 1.63, *P* = 0.001). An FBG goal setting of <6.1 before initiating BI was not associated with increased hypoglycemic incidence (OR = 0.97, 95% CI: 0.77 – 1.22, *P* = 0.789) or rate (RR = 0.92, 95% CI: 0.76 – 1.1, *P* = 0.349). For hypoglycemia defined as SMBG <3.0 mmol/L, 1,852 patients (15.2%) with 2,954 events were recorded, resulting in an incidence rate of 0.97 events per person-year. Similar trends were observed in relation to complications, duration of diabetes, and baseline HbA1c levels. An FBG goal of <6.1 was not related to increased incidence (OR = 0.97, 95% CI: 0.77 – 1.22, *P* = 0.789) or rate (RR: 1.01, 95% CI: 0.80 – 1.27, *P* = 0.953) of hypoglycemia (Table 6).

Table 5 Hypoglycemia incidence during 3 months in patients with SMBG

	N	Month 3	OR (95% CI)	*P*-value
SMBG ≤3.9 mmol/L				
All	12227	3317 (27.1)		
Patient sources				
Outpatient	4581	1177 (25.7)	Reference	
Inpatient	7646	2140 (28.0)	1.24 (1.07, 1.45)	0.005
Complication				
No	1962	469 (23.9)	Reference	
Yes	5125	1350 (26.3)	1.25 (1.07, 1.46)	0.005
Duration, years				
<5	5518	1803 (32.7)	Reference	
≥5	6709	1514 (22.6)	0.60 (0.52, 0.69)	<0.001
Baseline HbA1c, %				
7-8	1953	390 (20.0)	Reference	
8-9	2138	512 (23.9)	1.14 (0.94, 1.38)	0.1973
9-10	1787	461 (25.8)	1.26 (1.03, 1.55)	0.0233
≥10	3924	1276 (32.5)	1.47 (1.23, 1.76)	<.0001

FBG goal setting, mmol/L				
≥6.1	10422	2827 (27.1)	Reference	
<6.1	1777	484 (27.2)	0.98 (0.81, 1.17)	0.789
SMBG <3.0 mmol/L				
All	12227	1852 (15.2)		
Patient sources				
Outpatient	4581	702 (15.3)	Reference	
Inpatient	7646	1150 (15.0)	1.05 (0.87, 1.26)	0.639
Complication				
No	1962	249 (12.7)	Reference	
Yes	5125	753 (14.7)	1.26 (1.04, 1.54)	0.020
Duration, years				
<5	5518	1009 (18.3)	Reference	
≥5	6709	843 (12.6)	0.63 (0.53, 0.74)	<0.001
Baseline HbA1c, %				
7-8	1953	207 (10.6)	Reference	
8-9	2138	289 (13.5)	1.24 (0.97, 1.6)	0.092
9-10	1787	259 (14.5)	1.34 (1.03, 1.74)	0.027
≥10	3924	727 (18.5)	1.64 (1.3, 2.07)	<0.001
FBG goal setting, mmol/L				
≥6.1	10422	1584 (15.2)	Reference	
<6.1	1777	262 (14.7)	0.97 (0.77, 1.22)	0.789

Table 6 Hypoglycemia rates during 3 months in patients with SMBG

	No. of events	Events/person-year	RR (95% CI)	*P*-value
SMBG ≤3.9 mmol/L				
All	7619	2.49		
Patient sources				
Outpatient	2581	2.25	Reference	
Inpatient	5038	2.64	1.25 (1.08, 1.46)	0.004
Complication				
No	960	1.96	Reference	
Yes	2897	2.26	1.25 (1.07, 1.47)	0.006
Duration, years				
<5	4482	3.25	Reference	
≥5	3137	1.87	0.67 (0.59, 0.77)	<0.001
Baseline HbA1c, %				
7-8	871	1.78	Reference	
8-9	1098	2.05	1.00 (0.82, 1.21)	0.969
9-10	994	2.22	1.15 (0.94, 1.4)	0.184
≥10	3168	3.23	1.37 (1.15, 1.63)	0.001
FBG goal setting, mmol/L				
≥6.1	6449	2.48	Reference	
<6.1	1155	2.60	0.92 (0.76, 1.1)	0.349
SMBG <3.0 mmol/L				
All	2954	0.97		
Patient sources				
Outpatient	1138	0.99	Reference	
Inpatient	1816	0.95	1.06 (0.87, 1.29)	0.559
Complication				
No	366	0.75	Reference	
Yes	1156	0.90	1.24 (1.01, 1.52)	0.041
Duration, years				
<5	1691	1.23	Reference	
≥5	1263	0.75	0.66 (0.56, 0.79)	<0.001
Baseline HbA1c, %				
7-8	298	0.61	Reference	
8-9	456	0.85	1.34 (1.04, 1.72)	0.026

9-10	381	0.85	1.30 (0.99, 1.70)	0.056
≥10	1253	1.28	1.72 (1.36, 2.18)	<0.001
FBG goal setting, mmol/L				
≥6.1	2499	0.96	Reference	
<6.1	447	1.01	1.01 (0.80, 1.27)	0.953

Table 7 presents the composite endpoints of patients reaching the target without hypoglycemia events during a 3-month period. For HbA1c <7% without SMBG ≤3.9 mmol/L at month 3, patients with complications (OR = 0.68, 95% CI: 0.54 – 0.84, *P* = 0.001) and those with a duration of diabetes ≥5 years (OR = 0.76, 95% CI: 0.62 – 0.93, *P* = 0.008) had significantly lower odds of reaching the target without hypoglycemia events. Additionally, higher baseline HbA1c levels in the ranges of 9-10% (OR = 1.26, 95% CI: 1.03 – 1.55, *P* = 0.023) and ≥10% (OR = 1.47, 95% CI: 1.23 – 1.76, *P* < 0.001) were associated with increased odds of achieving the target. Also, those who set a FBG goal of <6.1 mmol/L at the time of initiation had significantly higher odds of achieving the composite endpoint (OR = 1.35, 95% CI 1.03 – 1.79, *P* = 0.033). For achieving FBG <7 mmol/L without SMBG ≤3.9 mmol/L at month 3, none of these factors were related to the composite endpoints. Finally, for achieving FBG <6.1 mmol/L without SMBG ≤3.9 mmol/L at month 3, only the duration of diabetes ≥5 years was associated with a significantly lower possibility of achieving this composite endpoint.

Table 7 Composite endpoints of patients reaching target without hypoglycemia events during 3 months in patients with SMBG

	N	Month 3	OR (95% CI)	*P*-value
HbA1c <7% without SMBG ≤3.9 mmol/L				
All	5121	2055 (40.1)		
Patient sources				
Outpatient	1987	750 (37.7)	Reference	
Inpatient	3134	1305 (41.6)	1.14 (0.92, 1.41)	0.228
Complication				
No	735	352 (47.9)	Reference	
Yes	1952	697 (35.7)	0.68 (0.54, 0.84)	0.001
Duration, years				
<5	2325	1024 (44.0)	Reference	
≥5	2796	1031 (36.9)	0.76 (0.62, 0.93)	0.008
Baseline HbA1c, %				
7-8	942	436 (46.3)	Reference	
8-9	881	319 (36.2)	1.14 (0.94, 1.38)	0.197
9-10	811	297 (36.6)	1.26 (1.03, 1.55)	0.023
≥10	1495	579 (38.7)	1.47 (1.23, 1.76)	<0.001
FBG goal setting, mmol/L				
≥6.1	4435	1735 (39.1)	Reference	

<6.1	686	320 (46.6)	1.35 (1.03, 1.79)	0.033
FBG <7 mmol/L without SMBG ≤3.9 mmol/L				
All	5988	2398 (40.0)		
Patient sources				
Outpatient	2203	883 (40.1)	Reference	
Inpatient	3785	1515 (40.0)	0.98 (0.81, 1.18)	0.796
Complication				
No	830	363 (43.7)	Reference	
Yes	2531	947 (37.4)	0.85 (0.7, 1.04)	0.112
Duration, years				
<5	2831	1197 (42.3)	Reference	
≥5	3157	1201 (38.0)	0.93 (0.78, 1.11)	0.408
Baseline HbA1c, %				
7-8	957	438 (45.8)	Reference	
8-9	1005	436 (43.4)	1.08 (0.85, 1.37)	0.525
9-10	897	326 (36.3)	0.94 (0.73, 1.20)	0.608
≥10	2050	807 (39.4)	0.94 (0.75, 1.17)	0.583
FBG goal setting, mmol/L				
≥6.1	5071	1989 (39.2)	Reference	
<6.1	905	406 (44.9)	1.06 (0.84, 1.33)	0.617
FBG <6.1 mmol/L without SMBG ≤3.9 mmol/L				
All	5988	1174 (19.6)		
Patient sources				
Outpatient	2203	438 (19.9)	Reference	
Inpatient	3785	736 (19.4)	0.83 (0.66, 1.04)	0.109
Complication				
No	830	194 (23.4)	Reference	
Yes	2531	434 (17.1)	0.81 (0.64, 1.03)	0.085
Duration, years				
<5	2831	643 (22.7)	Reference	
≥5	3157	531 (16.8)	0.74 (0.59, 0.92)	0.007
Baseline HbA1c, %				
7-8	957	213 (22.3)	Reference	
8-9	1005	198 (19.7)	1 (0.75, 1.34)	0.997
9-10	897	139 (15.5)	0.79 (0.58, 1.09)	0.151
≥10	2050	439 (21.4)	1.03 (0.79, 1.36)	0.818
FBG goal setting, mmol/L				
≥6.1	5071	955 (18.8)	Reference	
<6.1	905	218 (24.1)	0.97 (0.74, 1.29)	0.856

Discussion

Principle Results

The TRIO program, a large-scale health management initiative utilizing a digital WeChat platform for patients with T2DM initiating BI treatment, demonstrated its effectiveness in improving glycemic control at 3 months after initiating BI. Prior to enrollment in TRIO, T2DM patients enrolled exhibited suboptimal blood glucose control, with elevated baseline HbA1c (9.6%) and FPG (9.5 mmol/L), a high prevalence of diabetic complications and long diabetes duration (7.3 years). Following the 3-month TRIO management intervention, notable reductions in HbA1c (-2.59%) and

FBG (-2.77 mmol/L) were observed in the total population, accompanied by heightened proportions of achieving HbA1c <7.0% (55.6%) and FBG target <7.0 mmol/L (61.3%) and across diverse subgroups, such as patients from inpatient or outpatient care, patients with or without complications, patients with different length of diabetes duration, baseline HbA1c, and FBG goal setting. This study also highlights the potential for setting a lower FBG target (<6.1 mmol/L) at the initiation of BI compared to the traditional <7.0 mmol/L target. By setting a more rigorous FBG target <6.1 mmol/L, better glycemic control was achieved without increased risk of hypoglycemia. These results hold promise for digital health tool such as TRIO in improving the overall management of T2DM in real-world clinical settings.

TRIO has showed effectiveness and safety in T2DM patients initiating BI after OAD failure with the assistance of WeChat digital platform, which is consistent with previous single-arm studies incorporating digital tools conducted in prediabetes (15) (18) and patients treated with premixed insulin and BI (14) (19) (20). For instance, the Omada Health Program investigated digital Diabetes Prevention Program (DPP) engagement among prediabetic patients, showing a reduction of -0.33 mmol/L in HbA1c levels over three years (15). In our TRIO study, with a larger sample size, we achieved a greater HbA1c reduction of -2.58 mmol/L. Furthermore, in a 12-week German trial involving individuals with type 2 diabetes on basal insulin, a smartphone app (My Dose Coach) was compared to a written titration chart. The intervention group utilizing the app exhibited a noteworthy reduction in HbA1c levels compared to the control group (-0.31%; p = 0.0388), with safety outcomes remaining unaffected. These findings suggest that app-assisted titration can enhance glycemic control in patients with type 2 diabetes who use basal insulin (20).

TRIO has demonstrated that digital tools including health education and self-management modules added on basal insulin might provide additional benefit to effectiveness in glycemic control than medication alone. The ORBIT study is an observational registry conducted in China with T2DM patients who were inadequately controlled by OADs and initiated BI (21), with similar baseline

HbA1c (9.6 ± 2.0%), but higher baseline FBG (11.7 ± 4.0 mmol/L) and shorter diabetes duration (6.4 ± 5.3 years) than those in our study. Notably, the change in HbA1c from baseline to month 3 demonstrated a more improvement in the TRIO group (-2.59%) than in the ORBIT group (-2%), as well as the attainment of the HbA1c target <7% at month 3 (55.6% vs. 35.9%). Despite the relatively lower reduction in FBG levels in the TRIO study due to lower baseline FBG levels, a larger proportion of TRIO patients successfully reached the FBG target of <7 mmol/L (61.3%) compared to the ORBIT study (37.3%). Another significant study in this field, the First Basal Insulin Evaluation (FINE) Asia study, was a multinational, prospective, observational approach to assess basal insulin's efficacy in patients with uncontrolled type 2 diabetes (HbA1c ≥ 8%) (22).

In TRIO, baseline HbA1c and FBG were as high as 9.6% and 9.5 mmol/L, respectively (Table 1), which suggest delayed initiation of BI. The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) suggest that BI should be promptly considered after the apparent "failure" of lifestyle modifications, including diet and exercise in combination with metformin, particularly when HbA1c levels remain at or exceed 7.0% for a span of 2–3 months (23). However, consistent with our findings, delay in initiation of injectable therapies was universal (24,25). Timely initiation of insulin such as BI after failure of oral treatment is associated with better glycemic control (26).

Common T2DM management advice recommends keeping HbA1c levels below 7%, but the ideal FPG target for achieving this is debated (27). Different guidelines suggest varying FPG targets, such as 4.4-7.2 mmol/L according to the ADA 2018 guidelines (28) or <6.1 mmol/L according to the American Association of Clinical Endocrinologists-American College of Endocrinology and the International Diabetes Federation (29). Previous studies support a FPG target of 6.1 mmol/L, showing better outcomes. Patients with FPG goals below 6.1 mmol/L had greater HbA1c reductions and higher target achievement rates without an increase in hypoglycemia (30) (31). Our results might confirm a better FPG target of <6.1 mmol/L. Patients who had an initial FPG goal setting below 6.1

mmol/L by their physician at the time of enrolment experienced both greater reductions in their HbA1c levels (-2.64 vs. -2.57%) and a higher HbA1c target rate (67.8 vs. 53.1 %) compared to those with FPG goal setting ≥ 6.1 mmol/L (Tables 2-3). At the same time, hypoglycemic incidence and rate were comparable between the 2 groups.

Regarding the titration of basal insulin treatment, the current Chinese guideline recommends an initial dose of 0.2 U/kg or 10 U, underscoring the importance of active insulin dose adjustment to achieve optimal glycemic control (32). Previous studies like ORBIT have indicated inadequate titration, evident from a starting dose of 0.18 IU/kg/d and a final dose of 0.21 IU/kg/d, resulting in a change of +0.034 IU/kg/d. Within our program, comprehensive titration was not uniformly accomplished. Among the 36,307 patients with baseline and 3-month dosage data, 42.5% of patients escalated their dosage during the program, while 7% maintained stability and 49.7% decreased their dosage. Consequently, there was a marginal numerical decline in dose by -0.01 (0.06) U/kg. Plausible explanations for this trend encompass the higher-than-recommended starting dose in our program, which even surpassed the final doses in earlier ORBIT studies. Furthermore, the pursuit of targeted FBG levels in the initial weeks and an increased incidence of hypoglycemic events among patients (as shown in Table S3) could have contributed to these patterns.

Limitations

Our study supports TRIO's effectiveness and safety as a personalized health program, yet several limitations warrant acknowledgment. A significant portion of patients lacked HbA1c follow-up data at month 3, possibly introducing a compliance bias that could overstate TRIO's effectiveness by excluding those with less favorable HbA1c reductions. Nonetheless, comparable baseline characteristics between compliant and non-compliant patients mitigate the risk of overestimation. Long-term data (months 3 to 12) are insufficient, leaving uncertainty about TRIO's enduring effectiveness and ability to sustain patient adherence. Moreover, the observational nature of our study raises concerns about data credibility due to potential missing values and self-reporting

inaccuracies. The absence of a randomized controlled trial (RCT) design and an external control group underscores the need for future research to confirm TRIO's effectiveness, potentially through RCT or propensity score matching methods.

Conclusions

In conclusion, the TRIO program has demonstrated effectiveness in glycemic control, as reflected in HbA1c and FBG levels, among T2DM patients initiating basal insulin therapy. The program has improved HbA1c and FBG target rates and patient compliance with insulin treatments. Exploring FBG < 6.1 mmol/L as a potentially better target could further enhance glycemic control outcomes. However, it is important to acknowledge the limitations of our study, including compliance bias, insufficient long-term follow-up data, and the need for further investigation using rigorous study designs. Future research, such as randomized controlled trials, is warranted to validate the findings of our study and assess the generalizability of TRIO in real-world populations.

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Authors Contributions

WWM and DLZ carried out the studies, LXG, LXS and LC participated in collecting data, and CXL drafted the manuscript. LMC and YMX performed the statistical analysis and participated in its

design. HL, YZL and JY participated in the acquisition, analysis, or interpretation of data and drafted the manuscript. All authors have read and approved the final manuscript.

Conflict of interests

The authors declare that they have no competing interests.

Abbreviations

T2DM: type 2 diabetes mellitus

BI: basal insulin

FPG: fasting plasma glucose

PPG: Postprandial Glucose

OADs: oral antidiabetic drugs

SMBG: self-monitoring blood glucose

RCT: randomized controlled trial

BMI: Body Mass Index;

SBP: Systolic Blood Pressure

DBP: Diastolic Blood Pressure

LDL: Low-Density Lipoprotein

OR: odds ratio

RR: relative risk

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Supplementary Files

Figures

Flowchart of participating patient enrollment.