Original Paper

Effectiveness and Safety of the TRIO Optimal Health Management Program in Patients With Type 2 Diabetes Mellitus Initiating Basal Insulin Therapy: Prospective Observational Real-World Study

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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 patients with prediabetes, including 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 apps specifically designed for patients with type 2 diabetes mellitus (T2DM) initiating basal insulin (BI). Based on this, a data-based and artificial intelligence management system named "TRIO" was developed to provide patients with more personalized intervention methods in stages, in groups, and around the clock. TRIO assists doctors and nurses in achieving better blood glucose controls, truly carries out standardized management around patients, and allows them to have a higher quality of life. TRIO represents the 3 essential pillars in comprehensive diabetes management: physician, nurse, and patient.

Objective: This prospective observational study evaluated the effectiveness and safety of the TRIO optimal health management program for patients with T2DM initiating BI therapy in a real-world setting.

Methods: Patients aged 18-85 years with inadequate glycemic control (baseline hemoglobin A_{1c} [HbA_{1c}] ≥7%) starting BI therapy were enrolled in outpatient and inpatient settings. The study lasted 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 between December 1, 2019, and December 31, 2021, involving 574 hospitals in China. The mean baseline HbA_{1c} was 9.2%, the mean duration of diabetes was 7.3 years, and 80.4% (1,59,930/1,98,969) of patients were using BI with oral antihyperglycemic drugs. After the intervention, mean HbA_{1c} decreased by –2.59% from baseline, with 55.6% (28,858/51,912) achieving the target HbA_{1c} level of <7%. Patients who set lower fasting plasma glucose goals (<6.1 mmol/L) showed more significant HbA_{1c} reductions (P<.001) and higher target achievement than those with fasting plasma glucose goals of ≥6.1 mmol/L. Factors such as complications, diabetes duration, and baseline HbA_{1c} levels influenced the magnitude of HbA_{1c} reduction. The presence of complications, shorter diabetes duration, and higher baseline HbA_{1c} were significantly associated with increased hypoglycemia incidence risk (all P<.05).

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

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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 rapidly increasing due to lifestyle changes and an aging population. As per the 2018 American Diabetes Association 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% (10,071/30,609) of patients with diabetes received treatment, with only half of them (15,336/30,609, 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 (BI), 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 pivotal. This involves the appropriate titration of insulin and 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 patients with type 2 diabetes [8]. The lack of comprehensive and patient-centered approaches in current health care systems further compounds the burden of diabetes management. Time constraints and resource availability often limit traditional health education and face-to-face interactions with health care 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 apps and WeChat miniprograms has increased application in diverse therapeutic domains, such as attention-deficit/hyperactivity disorder, cancer, asthma, and insomnia tools to augment patient self-management [12].

Objectives

The potential of digital therapeutics for diabetes has garnered recognition from different organizations, such as the Centers for Disease Control and Prevention and the Digital Therapeutics Alliance [13]. Although some prior studies have demonstrated successful reductions in patients' blood glucose levels and body weight through digital diabetes programs up to a hemoglobin A_{1c} (HbA_{1c}) reduction of 0.49% [14], many studies were limited by including patients with prediabetes [15], including 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 apps specifically designed for patients with T2DM initiating BI.

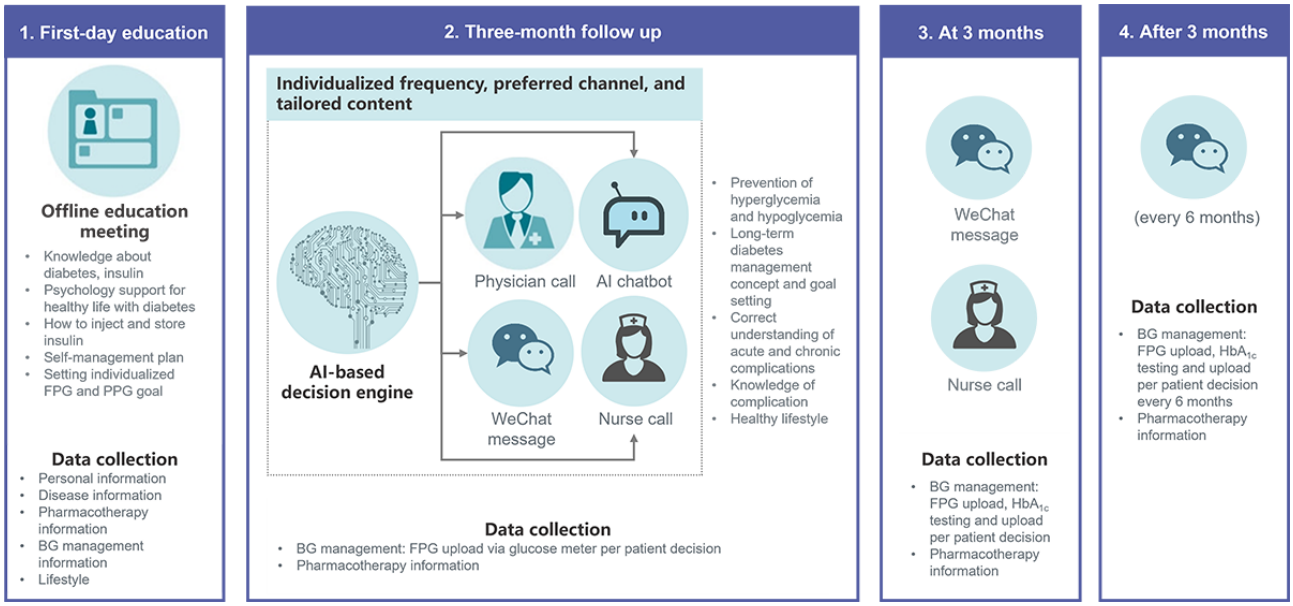
Accordingly, we have developed a personalized health management program combined with artificial intelligence named "TRIO" for initiating BI therapy in patients with type 2 diabetes and aim to evaluate its effectiveness and safety. Unlike conventional acronyms or abbreviations, TRIO does not represent a longer phrase but rather represents the 3 essential pillars in comprehensive diabetes management: physician, nurse, and patient. This program combines traditional health education with a mobile app to enhance diabetes management. Through this evaluation, we aspire to contribute to understanding practical approaches to 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 departments and, at discharge, from inpatient departments between December 1, 2019, and December 31, 2021, from 594 hospitals in China. Patients were assessed for their suitability by the following criteria: (1) aged between 18 and 85 years; (2) patients with T2DM who were inadequately controlled by OADs at the time of enrollment (ie, baseline HbA_{1c} level of ≥7%); (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; and (5) absence of severe illnesses or limitations regarding follow-up. Patients who fulfilled these eligibility requirements were enrolled upon their willingness to provide informed consent. On the first day of enrollment, patients received health education from nurses, including knowledge about diabetes and insulin, psychological support for a healthy life with diabetes, and how to inject and store insulin. In addition, the physicians assisted patients in drawing up a self-management plan and helped them set individualized fasting plasma glucose (FPG) and postprandial glucose (PPG) goals. 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 level was 7 mmol/L, a phone call was not scheduled for the next follow-up visit, and only a WeChat message was sent (Figure 1).

Figure 1. The operating process of the TRIO optimal health management program. AI: artificial intelligence; BG: blood glucose; FPG: fasting plasma glucose; HbA_{1c}: hemoglobin A1c; PPG: postprandial glucose.



Ethical Considerations

This study was approved by the ethics committee of Nanjing Drum Tower Hospital (institutional review board review approval document, code: 2019-231-01), which was the principal research institute representing other subcenters. Implied consent was obtained from all participants when they registered on the TRIO WeChat official account following the principles of the Declaration of Helsinki, as the privacy policy included a clause allowing anonymized data to be used for research purposes. Participant privacy and anonymity were achieved through the elimination of any patient identifiers such as name or dates of birth, which were anonymized and deidentified before extraction and securely stored in compliance with data protection regulations. No compensation was provided to participants, as this study involved a secondary analysis of existing data. No identifiable images of participants were included in the study or supplementary materials, eliminating the need for additional image consent.

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, glucagon-like peptide-1 receptor agonists, or OAD) used with BI. Laboratory tests including HbA_{1c} and FPG were obtained in hospitals at baseline, while glycemic control regarding HbA_{1c} 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 end points*: The primary effectiveness end point of our analysis is the change in HbA_{1c} levels from baseline to month 3.

- *Secondary effectiveness end points*: In addition to the primary end point, we also examined various other measures related to glycemic control. These secondary end points include changes in FBG levels from baseline to month 3, the achievement of target HbA_{1c}levels (<7%), the achievement of target FBG levels (<7 and <6.1 mmol/L), and an assessment of changes in BI dose.
- *Safety end points*: Our safety end points include monitoring and assessing the incidence and rates of hypoglycemia events and evaluating composite end points. The 3-month end point included the incidence and rates of hypoglycemia events and a composite end point encompassing the percentage of patients reaching target HbA_{1c} and FBG levels without experiencing hypoglycemia events.

Statistical Methods

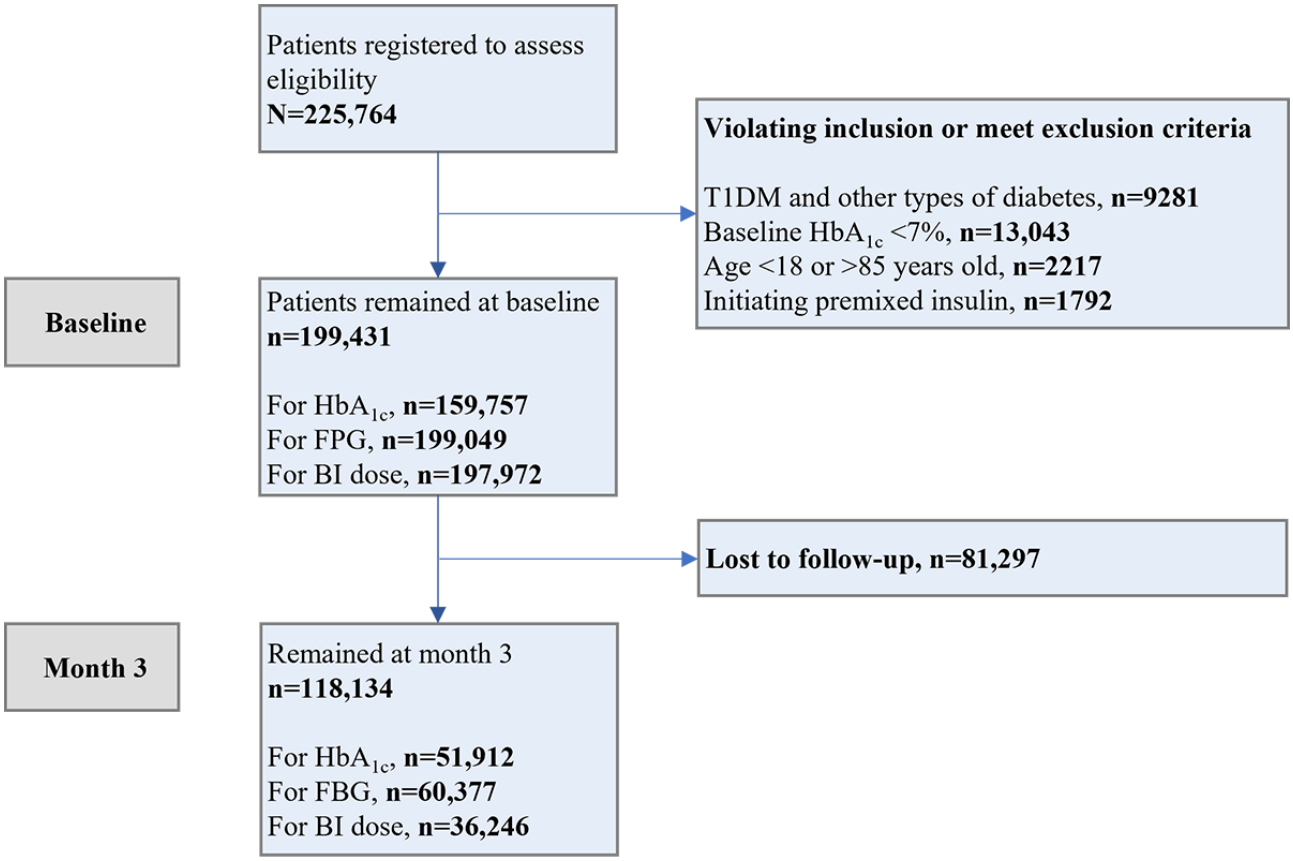
Continuous variables were described using mean and SD, while categorical variables were presented as frequencies and percentages. For continuous effectiveness indicators, a paired *t* test (2-tailed) was applied to test the significance of the change from baseline to month 3 in HbA_{1c} or FPG in the total population. Analysis of covariance was used to compare these changes between subgroups, including patient source (inpatient or outpatient), complication status (no or yes), duration of diabetes (<5 years or ≥5 years), baseline HbA_{1c} (7%-8%, 8%-9%, 9%-10%, or ≥10%), and FBG goal setting (≥6.1 mmol/L or <6.1 mmol/L). Least square (LS) mean (SE) and LS mean difference with 95% CIs were provided. For binary effectiveness outcomes (HbA_{1c} <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 analysis of covariance model. Hypoglycemic incidence and rate were evaluated by 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 95% CI was used as the effect size; hypoglycemic rate (numbers of events per patient-year) was investigated by Poisson regression, and risk ratio (RR) with 95% CI were used as the effect size for this analysis. Composite end points including HbA_{1c} <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), and a 2-sided *P* value of <.05 was considered statistically significant.

Results

Participant Recruitment

Between December 1, 2019, and December 31, 2021, a total of 225,764 patients were recruited from 594 hospitals. A total of 26,333 patients were excluded because of violating inclusion or meeting exclusion criteria, leaving 199,431 patients remaining at baseline. Among them, 81,297 patients were lost to follow-up within the first 3 months, resulting in 118,134 patients who completed the 3-month follow-up with measurements of either HbA_{1c} or FPG (Figure 2).

Figure 2. Flowchart of participating patients enrolled in the TRIO optimal health management program. Nested values under "Patients remained at baseline" and "Remained at month 3" are non-mutually exclusive. BI: basal insulin; FPG: fasting plasma glucose; HbA_{1c}: hemoglobin A1c; T1DM: type 1 diabetes mellitus.



Baseline Characteristics

The patients' mean (SD) age at baseline was 57.3 (12.5) years, with 42.8% (85,337/1,99,431) of participants being women. The average BMI was 24.8 kg/m^2. At baseline, the mean HbA_{1c}, 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 (55,637/1,96,023, 28.4%), hyperlipidemia (32,240/1,96,023, 16.4%), and peripheral neuropathy (63,145/1,96,023, 32.2%). Most patients were taking BI with oral antihyperglycemic drugs (OADs) (1,59,930/1,98,969, 80.4%), with some also using prandial insulin concurrently.

Outpatients had a slightly higher mean age of 57.7 (SD 12.2) years than inpatients, with a mean age of 57.0 (SD 12.6) years. Gender distribution revealed that 56.3% (39,802/70,704) of outpatients were male, while 57.6% (74,064/1,28,645) of inpatients were male. Moreover, the duration of diabetes was slightly longer in inpatients, with a mean of 7.4 years (SD 6.8) than in outpatients, with a mean of 7.0 years (SD 6.3). Both groups displayed a similar average BMI of 24.8 kg/m^2 and exhibited comparable values for blood pressure and lipid levels such as triglycerides, total cholesterol, low-density lipoprotein, and baseline HbA_{1c}. Meanwhile, baseline FPG (10.3 vs 9.0 mmol/L) and PPG (14.0 vs 12.2 mmol/L) were slightly higher in outpatients than in inpatients. A notable difference was observed in the percentage of patients with complications or comorbidities, with 31.3% (39,950/1,27,610) of inpatients having hypertension compared with 22.9% (15,687/68,413) of outpatients and 38.1% (48,580/1,27,610) of inpatients having peripheral neuropathy compared with 21.3% (14,565/68,413) of outpatients. Inpatients also had a higher proportion of patients being treated with BI in combination with prandial insulin, accounting for 20.3% (26,037/1,28,342) of inpatients as opposed to 15.5% (10,924/70,627) of outpatients (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 S1 in Multimedia Appendix 1).

Table 1. Baseline characteristics of patients enrolled in the TRIO optimal health management program.

Baseline characteristics	Outpatient (n=70,786)	Inpatient (n=128,645)	All (N=199,431)
Age (years), mean (SD)	57.7 (12.2)	57.0 (12.6)	57.3 (12.5)
Sex, n (%)			
Male	39,802 (56.3)	74,064 (57.6)	1,13,866 (57.2)
Female	30,902 (43.7)	54,435 (42.4)	85,337 (42.8)
BMI (kg/m^2), mean (SD)	24.8 (3.3)	24.8 (3.5)	24.8 (3.5)
Duration of diabetes (years), mean (SD)	7.0 (6.3)	7.4 (6.8)	7.3 (6.6)
SBP[a] (mm Hg), mean (SD)	131.8 (15.4)	131.8 (16.5)	131.8 (16.2)
DBP[b] (mm Hg), mean (SD)	79.9 (10.1)	79.6 (10.4)	79.7 (10.3)
Triglycerides (mmol/L), mean (SD)	2.3 (2.0)	2.3 (2.1)	2.3 (2.1)
Total cholesterol (mmol/L), mean (SD)	4.6 (1.5)	4.7 (1.5)	4.7 (1.5)
LDL[c] (mmol/L), mean (SD)	2.8 (1.1)	2.8 (1.1)	2.8 (1.1)
BI[d] dose (U/d), mean (SD)	15.2 (5.5)	16.2 (6.1)	15.9 (5.9)
BI dose (U/kg/d), mean (SD)	0.23 (0.08)	0.24 (0.09)	0.24 (0.09)
eGFR[e] (mL/min/1.73 m^2), mean (SD)			
<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)	11,366 (51.2)
Baseline HbA_{1c}[f] (%), mean (SD)	9.3 (1.8)	9.7 (2.1)	9.6 (2.0)
Baseline FPG[g] (mmol/L), mean (SD)	10.3 (3.3)	9.0 (3.2)	9.5 (3.3)
Baseline PPG[h] (mmol/L), mean (SD)	14.0 (4.4)	12.2 (4.0)	12.7 (4.2)
Regimen, n (%)			
BI alone ± OAD[i]	59,176 (83.8)	1,00,754 (78.5)	1,59,930 (80.4)
BI + prandial insulin ± OAD	10,924 (15.5)	26,037 (20.3)	36,961 (18.6)
BI + GLP-1 RA[j] ± OAD	527 (0.7)	1551 (1.2)	2078 (1.0)
Comorbidity, n (%)			
Hypertension	15,687 (22.9)	39,950 (31.3)	55,637 (28.4)
Hyperlipemia	8992 (13.1)	23,248 (18.2)	32,240 (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, n (%)			
Stroke	1409 (2.1)	4511 (3.5)	5920 (3.0)
Coronary heart disease	4601 (6.7)	11,656 (9.1)	16,527 (8.3)
Diabetic nephropathy	3266 (4.8)	11,209 (8.8)	14,475 (7.4)
Diabetic retinopathy	6058 (8.9)	17,329 (13.6)	23,387 (11.9)
Diabetic foot	663 (1.0)	3253 (2.6)	3916 (2.0)
Peripheral neuropathy	14,565 (21.3)	48,580 (38.1)	63,145 (32.2)
Lower extremity angiopathy	2844 (4.2)	10,601 (8.3)	13,445 (6.9)

[a]SBP: systolic blood pressure.

[b]DBP: diastolic systolic blood pressure.

[c]LDL: low-density lipoprotein.

[d]BI: basal insulin.

[e]eGFR: estimated glomerular filtration rate.

[f]HbA_{1c}: hemoglobin A_{1c}.

[g]FPG: fasting plasma glucose.

[h]PPG: postprandial glucose.

[i]OAD: oral antidiabetic drug.

[j]GLP-1 RA: glucagon-like peptide-1 receptor agonists.

Initial Regimens and Adherence to BI Treatment

During the intervention, the majority of patients initiated insulin glargine (1,77,331/1,98,969, 89.1%) as their primary treatment, while a smaller proportion started with insulin determir (6588/1,98,969, 3.3%), neutral protamine Hagedorn insulin (766/1,98,969, 0.4%), or insulin degludec (8939/1,98,969, 4.5%). Alongside BI treatment, 41% (57,242/1,39,739), 28.2% (39,473/1,39,739), and 9.7% (13,545/1,39,739) of patients were concurrently taking 1, 2, and ≥3 OADs, respectively. The most commonly used OADs were metformin (69,027/1,39,739, 49.4%) and α-glucosidase inhibitors (46,960/1,39,739, 33.6%), followed by sodium-glucose cotransporter-2 inhibitors (22,911/1,39,739, 16.4%), dipeptidyl peptidase-4 inhibitors (20,722/1,39,739, 14.8%), sulfonylureas (7266/1,39,739, 5.2%), glinides (6257/1,39,739, 4.5%), and thiazolidinediones (5504/1,39,739, 3.9%). Sulfonylureas were more frequently prescribed to outpatients (3571/48,696, 7.3%) than inpatients (3695/91,043, 4.1%), while sodium-glucose cotransporter-2 inhibitors were more commonly used in inpatients (16,615/91,043, 18.2%) than outpatients (6296/48,696, 12.9%; Table S2 in Multimedia Appendix 1).

Glycemic Outcomes

At the end of the 3-month management intervention period, the mean HbA_{1c} level among 44,847 participants with eligible self-reported mean HbA_{1c} measurements was 6.89% (SD 0.90). This represented a mean decrease in HbA_{1c} by –2.59% (SE 0.01; P<.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 (SD 1.4) mmol/L, indicating an average decrease in FBG by –2.77 (SD 0.01) mmol/L (P<.001) from baseline (Table 2 and Figure S1 in Multimedia Appendix 1). For the HbA_{1c} target, 55.6% (28,858/51,912) of participants achieved the target HbA_{1c} level of <7% after the 3-month intervention period (Table 3). Similarly, 61.3% (37,017/60,377) and 29.2% (17,633/60,377) of participants reached FBG levels of <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 slightly lower HbA_{1c} (LS mean difference: 0.07, 95% CI 0.05-0.09) than those with no complications. Considering the duration of diabetes, patients with a duration of ≥5 years exhibited a lesser decrease in HbA_{1c} (LS mean difference: 0.09, 95% CI 0.07-0.11) than those with a duration of <5 years. A higher baseline HbA_{1c} level was also associated with a more significant reduction. Compared with patients with baseline HbA_{1c} in the range of 7% to 8%, patients with a baseline HbA_{1c} in the range of 8% to 9% had the lesser decrease (LS mean difference: –0.83, 95% CI –0.86 to –0.79), while patients with a baseline HbA_{1c} of 10% or higher had the highest decrease (LS mean difference: –4.04, 95% CI –4.08 to –4.00). Also, patients with initial FBG goal setting of <6.1 mmol/L had a greater decrease in their HbA_{1c} (LS mean difference: –0.36, 95% CI –0.38 to –0.34) than those with FBG goal setting of ≥6.1 mmol/L (Table 2). In the subgroup analysis exploring factors related to FBG reduction, consistent results with HbA_{1c} reductions found that more significant reductions were seen in patients with no complications, diabetes duration of <5 years, and an initial FBG goal setting of <6.1 mmol/L, except for baseline HbA_{1c}. Patients with lower baseline HbA_{1c} exhibited higher reductions in FBG from baseline (Table 2).

Table 2. HbA_{1c}[a] and fasting blood glucose change from baseline to month 3 after initiation of basal insulin therapy with TRIO monitoring.

	Values, n	Baseline, mean (SD)	Month 3, mean (SD)	LS[b] mean (SE)	*P* value	LS mean difference (95% CI)	*P* value
HbA_{1c} change from baseline to month 3							
All	44,847	9.48 (1.98)	6.89 (0.90)	–2.59 (0.01)	<.001	N/A[c]	
Patient sources							
Outpatient	14,893	9.10 (1.71)	6.93 (0.81)	–2.63 (0.02)	<.001	Reference	
Inpatient	29,954	9.67 (2.07)	6.88 (0.95)	–2.71 (0.01)	<.001	–0.08 (–0.1 to –0.06)	<.001
Complication							
No	17,963	9.33 (1.89)	6.83 (0.85)	–2.71 (0.02)	<.001	Reference	
Yes	20,389	9.58 (2.01)	6.96 (0.93)	–2.64 (0.01)	<.001	0.07 (0.05 to 0.09)	<.001
Duration (years)							
<5	18,950	9.69 (2.14)	6.80 (0.88)	–2.72 (0.02)	<.001	Reference	
≥5	25,888	9.32 (1.83)	6.96 (0.92)	–2.63 (0.01)	<.001	0.09 (0.07 to 0.11)	<.001
Baseline HbA_{1c} (%)							
7-8	9250	7.42 (0.33)	6.78 (0.88)	–0.79 (0.02)	<.001	Reference	
8-9	12,485	8.34 (0.32)	6.86 (0.89)	–1.62 (0.02)	<.001	–0.83 (–0.86 to –0.79)	<.001
9-10	8342	9.35 (0.31)	6.94 (0.86)	–2.54 (0.01)	<.001	–1.75 (–1.79 to –1.70)	<.001
≥10	14,770	11.81 (1.57)	6.97 (0.95)	–4.83 (0.02)	<.001	–4.04 (–4.08 to –4.00)	<.001
FBG[d] goal setting (mmol/L)							
≥6.1	36,935	9.54 (1.98)	6.96 (0.87)	–2.49 (0.01)	<.001	Reference	
<6.1	7904	9.22 (1.96)	6.58 (0.99)	–2.85 (0.02)	<.001	–0.36 (–0.38 to –0.34)	<.001
FBG change from baseline to month 3							
All	60,365	9.58 (3.30)	6.81 (1.40)	–2.77 (0.01)	<.001	N/A	
Patient sources							
Outpatient	21,055	10.35 (3.27)	6.86 (1.39)	–2.61 (0.02)	<.001	Reference	
Inpatient	39,310	9.17 (3.25)	6.79 (1.41)	–2.68 (0.02)	<.001	–0.07 (–0.09 to –0.04)	<.001
Complication							
No	22,927	9.86 (3.16)	6.68 (1.32)	–2.71 (0.02)	<.001	Reference	
Yes	28,252	9.14 (3.17)	6.94 (1.45)	–2.58 (0.02)	<.001	0.13 (0.11 to 0.16)	<.001
Duration (years)							
<5	24,683	9.74 (3.54)	6.57 (1.27)	–2.78 (0.02)	<.001	Reference	
≥5	35,666	9.48 (3.13)	6.98 (1.46)	–2.50 (0.02)	<.001	0.28 (0.25 to 0.3)	<.001
Baseline HbA_{1c} (%)							
7-8	10,005	8.35 (2.13)	6.68 (1.26)	–2.75 (0.02)	<.001	Reference	
8-9	13,472	9.21 (2.48)	6.79 (1.29)	–2.66 (0.02)	<.001	0.08 (0.05 to 0.12)	<.001

	Values, n	Baseline, mean (SD)	Month 3, mean (SD)	LS[b] mean (SE)	*P* value	LS mean difference (95% CI)	*P* value
9-10	9506	9.59 (2.99)	6.85 (1.39)	–2.61 (0.02)	<.001	0.13 (0.09 to 0.17)	<.001
≥10	18,879	10.32 (4.11)	6.83 (1.49)	–2.58 (0.01)	<.001	0.16 (0.13 to 0.20)	<.001
FBG goal setting (mmol/L)							
≥6.1	50,482	9.68 (3.32)	6.87 (1.40)	–2.52 (0.02)	<.001	Reference	
<6.1	9854	9.10 (3.18)	6.53 (1.35)	–2.76 (0.02)	<.001	–0.24 (–0.28 to –0.21)	<.001

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]LS: least squares.

[c]N/A: not applicable.

[d]FBG: fasting blood glucose.

Table 3. Target HbA_{1c}[a] and fasting blood glucose at month 3 after initiation of basal insulin therapy with TRIO monitoring.

	Values, n	Month 3, n (%)	OR[b] (95% CI)	*P* value
HbA_{1c} (<7% at month 3)				
All	51,912	28,858 (55.6)	N/A[c]	
Patient sources				
Outpatient	18,753	10,024 (53.5)	Reference	
Inpatient	33,159	18,834 (56.8)	1.16 (1.11-1.21)	<.001
Complication				
No	20,881	12,433 (59.5)	Reference	
Yes	23,008	12,016 (52.2)	0.85 (0.81-0.89)	<.001
Duration (years)				
<5	21,873	13,388 (61.2)	Reference	
≥5	30,030	15,466 (51.5)	0.83 (0.79-0.87)	<.001
Baseline HbA_{1c} (%)				
7-8	9250	5573 (60.2)	Reference	
8-9	12,485	6974 (55.9)	0.85 (0.8-0.9)	<.001
9-10	8342	4455 (53.4)	0.77 (0.72-0.83)	<.001
≥10	14,770	8009 (54.2)	0.72 (0.68-0.77)	<.001
FBG[d] goal setting (mmol/L)				
≥6.1	43,051	22,857 (53.1)	Reference	
<6.1	8845	5993 (67.8)	1.8 (1.7-1.9)	<.001
FBG (<7 mmol/L at month 3)				
All	60,377	37,017 (61.3)	N/A	
Patient sources				
Outpatient	21,065	12,403 (58.9)	Reference	
Inpatient	39,312	24,614 (62.6)	1.17 (1.12-1.22)	<.001
Complication				
No	22,936	14,952 (65.2)	Reference	
Yes	28,254	16,239 (57.5)	0.84 (0.8-0.88)	<.001
Duration (years)				
<5	24,686	17,053 (69.1)	Reference	
≥5	35,675	19,955 (55.9)	0.70 (0.67-0.73)	<.001
Baseline HbA_{1c} (%)				
7-8	10,006	6607 (66.0)	Reference	
8-9	13,473	8288 (61.5)	0.84 (0.79-0.89)	<.001
9-10	9509	5710 (60.0)	0.79 (0.74-0.85)	<.001
≥10	18,881	11,632 (61.6)	0.77 (0.73-0.82)	<.001
FBG goal setting (mmol/L)				
≥6.1	50,493	30,112 (59.6)	Reference	
<6.1	9855	6886 (69.9)	1.42 (1.34-1.5)	<.001
FBG (<6.1 mmol/L at month 3)				
All	60,377	17,633 (29.2)	N/A	
Patient sources				

	Values, n	Month 3, n (%)	OR[b] (95% CI)	*P* value
Outpatient	21,065	5763 (27.4)	Reference	
Inpatient	39,312	11,870 (30.2)	1.16 (1.1-1.22)	<.001
Complication				
No	22,936	7542 (32.9)	Reference	
Yes	28,254	7087 (25.1)	0.83 (0.79-0.87)	<.001
Duration (years)				
<5	24,686	8973 (36.3)	Reference	
≥5	35,675	8656 (24.3)	0.7 (0.66-0.73)	<.001
Baseline HbA_{1c} (%)				
7-8	10,006	3167 (31.7)	Reference	
8-9	13,473	3764 (27.9)	0.84 (0.79-0.9)	<.001
9-10	9509	2625 (27.6)	0.87 (0.81-0.93)	<.001
≥10	18,881	5746 (30.4)	0.91 (0.85-0.96)	.002
FBG goal setting (mmol/L)				
≥6.1	50,493	13,538 (26.8)	Reference	
<6.1	9855	4084 (41.4)	1.7 (1.62-1.8)	<.001

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]OR: odds ratio.

[c]N/A: not applicable.

[d]FBG: fasting blood glucose.

Regarding target HbA_{1c} of <7% at month 3, patients enrolled from inpatient showed a slight advantage over outpatient (OR 1.16, 95% CI 1.11-1.21; *P*<.001), and patients with complications had lower odds of achieving HbA_{1c} target than those with no complications (OR 0.85, 95% CI 0.81-0.89; *P*<.001). Those with ≥5 years of duration of diabetes had lower success rates than those with <5 years of duration (OR 0.83, 95% CI 0.79-0.87; *P*<.001). Lower baseline HbA_{1c} levels were associated with better outcomes. Moreover, setting FBG target goal level of <6.1 mmol/L at the beginning of the treatment demonstrated a higher possibility of reaching the HbA_{1c} target of <7% at month 3 (OR 1.8, 95% CI 1.7-1.9; *P*<.001) (Table 3). Regarding the FBG target of <7 and <6.1 mmol/L at month 3, patients exhibited consistent results as in HbA_{1c} target of <7%. Inpatients; patients with no complications; and patients with diabetes duration of 5 years, lower HbA_{1c} target, and initial FBG goal setting of <6.1 mmol/L were associated with higher odds of achieving the target (Table 3).

Insulin Dose and Satisfaction

Total insulin dose (U/d/kg) change was –0.01 (SD 0.06), from baseline (mean 0.23, SD 0.09) to month 3 (mean 0.22, SD 0.09; Table 4). Patients recruited from inpatients, with complications, having diabetes duration of ≥5 years, with FBG goal setting of <6.1 mmol/L and higher baseline HbA_{1c}, had a higher starting dose of BI. Among 36,037 patients with both baseline and 3-month BI dosages, 7% (2546/36,037) remained unchanged, and 50.1% (18,047/36,037) lowered the dosage per kilogram (Table 4). Possible reasons for the lack of titration, such as patients reaching FBG targets or experiencing hypoglycemic events, were explored in Table S3 in Multimedia Appendix 1. Patients with stable or decreasing dosage during the 3 months had higher starting doses, higher percentages of FBG <7 mmol/L, and hypoglycemic incidence at week 1, 2, 4, 8, and 12 than patients with increasing dosage. Patient satisfaction level for TRIO was stable during the study. Furthermore, 99.6% (35,738/35,897) of the patients felt satisfactory or very satisfactory at month 3, and only 0.4% (159/35,897) chose average or below.

Table 4. Basal insulin dose (U/kg) change from baseline to month 3 by patient sources, with or with no complication, duration, baseline HbA_{1c}[a] levels, and target fasting plasma glucose levels.

	Values, n	Baseline, mean (SD)	Month 3, mean (SD)	Change, mean (SD)
All	36,037	0.23 (0.09)	0.22 (0.09)	–0.01 (0.06)
Patient sources				
Outpatient	12,999	0.22 (0.08)	0.22 (0.08)	0.00 (0.05)
Inpatient	23,038	0.24 (0.09)	0.23 (0.09)	–0.01 (0.06)
Complication				
No	17,903	0.23 (0.08)	0.22 (0.08)	–0.01 (0.06)
Yes	17,163	0.24 (0.09)	0.23 (0.09)	–0.01 (0.06)
Duration (years)				
<5	13,993	0.22 (0.08)	0.21 (0.09)	–0.01 (0.06)
≥5	22,034	0.24 (0.09)	0.23 (0.09)	0.00 (0.05)
Baseline HbA_{1c} (%)				
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	11,003	0.24 (0.09)	0.23 (0.09)	–0.02 (0.06)
FBG[b] goal setting (mmol/L)				
≥6.1	30,034	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	15,444	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	18,047	0.25 (0.09)	0.21 (0.09)	–0.04 (0.06)

[a]HbA_{1c}: hemoglobin A_{1c}.

[b]FBG: fasting blood glucose.

Incidence and Event Rate of Hypoglycemia

Hypoglycemia incidence (≤3.9 mmol/L) in all patients was 27.1% (3317/12,227). Inpatients had a higher incidence than outpatients (OR 1.24, 95% CI 1.07-1.45; *P*=.005). Patients with complications experienced more hypoglycemia (OR 1.25, 95% CI 1.07-1.45; *P*=.005). Longer diabetes duration (≥5 years) was associated with lower hypoglycemia incidence (OR 0.60, 95% CI 0.52-0.69; *P*<.001; Table 5). Higher baseline HbA_{1c} levels correlated with increased hypoglycemia risk. HbA_{1c} ≥10% had the highest incidence (OR 1.47, 95% CI 1.23-1.76; *P*<.001; Table 5). For hypoglycemic events defined by SMBG levels of ≤3.9 mmol/L, a total of 7619 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 with outpatient sources (RR 1.25, 95% CI 1.08-1.46; *P*=.004), higher rates in patients with complications compared with those with no complications (RR 1.25, 95% CI 1.07-1.47; *P*=.006), and a lower rate in patients with a diabetes duration of ≥5 years (RR=0.67, 95% CI 0.59-0.77; *P*<.001). Furthermore, elevated baseline HbA_{1c} levels (≥10%) were associated with a higher hypoglycemia rate (RR 1.37, 95% CI 1.15-1.63; *P*=.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*=.79) or rate (RR 0.92, 95% CI 0.76-1.1; *P*=.35). For hypoglycemia defined as SMBG <3.0 mmol/L, 15.1% (1852/12,227) of patients with 2954 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 HbA_{1c} levels. An FBG goal of <6.1 was not related to increased incidence (OR 0.97, 95% CI 0.77-1.22; *P*=.79) or rate (RR 1.01, 95% CI 0.80-1.27; *P*=.95) of hypoglycemia (Table 6).

Table 5. Hypoglycemia incidence during 3 months of TRIO monitoring in patients with self-monitoring blood glucose.

	Values, n	Month 3, n (%)	OR[a] (95% CI)	*P* value
SMBG[b] (≤3.9 mmol/L)				
All	12,227	3317 (27.1)	N/A[c]	
Patient sources				
Outpatient	4581	1177 (25.7)	Reference	
Inpatient	7646	2140 (28.0)	1.24 (1.07-1.45)	.005
Complication				
No	1962	469 (23.9)	Reference	
Yes	5125	1350 (26.3)	1.25 (1.07-1.46)	.005
Duration (years)				
<5	5518	1803 (32.7)	Reference	
≥5	6709	1514 (22.6)	0.60 (0.52-0.69)	<.001
Baseline HbA_{1c}[d] (%)				
7-8	1953	390 (20.0)	Reference	
8-9	2138	512 (23.9)	1.14 (0.94-1.38)	.20
9-10	1787	461 (25.8)	1.26 (1.03-1.55)	.02
≥10	3924	1276 (32.5)	1.47 (1.23-1.76)	<.001
FBG[e] goal setting (mmol/L)				
≥6.1	10,422	2827 (27.1)	Reference	
<6.1	1777	484 (27.2)	0.98 (0.81-1.17)	.79
SMBG (<3.0 mmol/L)				
All	12,227	1852 (15.2)	N/A	
Patient sources				
Outpatient	4581	702 (15.3)	Reference	
Inpatient	7646	1150 (15.0)	1.05 (0.87-1.26)	.64
Complication				
No	1962	249 (12.7)	Reference	
Yes	5125	753 (14.7)	1.26 (1.04-1.54)	.02
Duration (years)				
<5	5518	1009 (18.3)	Reference	
≥5	6709	843 (12.6)	0.63 (0.53-0.74)	<.001
Baseline HbA_{1c} (%)				
7-8	1953	207 (10.6)	Reference	
8-9	2138	289 (13.5)	1.24 (0.97-1.6)	.09
9-10	1787	259 (14.5)	1.34 (1.03-1.74)	.03
≥10	3924	727 (18.5)	1.64 (1.3-2.07)	<.001
FBG goal setting (mmol/L)				
≥6.1	10,422	1584 (15.2)	Reference	
<6.1	1777	262 (14.7)	0.97 (0.77-1.22)	.79

[a]OR: odds ratio.

[b]SMBG: self-monitoring blood glucose.

[c]N/A: not applicable.

[d]HbA_{1c}: hemoglobin A_{1c}.

[e]FBG: fasting blood glucose.

Table 6. Hypoglycemia rates during 3 months of TRIO monitoring in patients with self-monitoring blood glucose.

	Events, n	Events/person-year	RR[a] (95% CI)	*P* value
SMBG[b] (≤3.9 mmol/L)				
All	7619	2.49	N/A[c]	
Patient sources				
Outpatient	2581	2.25	Reference	
Inpatient	5038	2.64	1.25 (1.08-1.46)	.004
Complication				
No	960	1.96	Reference	
Yes	2897	2.26	1.25 (1.07-1.47)	.006
Duration (years)				
<5	4482	3.25	Reference	
≥5	3137	1.87	0.67 (0.59-0.77)	<.001
Baseline HbA_{1c}[d] (%)				
7-8	871	1.78	Reference	
8-9	1098	2.05	1.00 (0.82-1.21)	.97
9-10	994	2.22	1.15 (0.94-1.4)	.18
≥10	3168	3.23	1.37 (1.15-1.63)	.001
FBG[e] goal setting (mmol/L)				
≥6.1	6449	2.48	Reference	
<6.1	1155	2.60	0.92 (0.76-1.1)	.35
SMBG (<3.0 mmol/L)				
All	2954	0.97	N/A	
Patient sources				
Outpatient	1138	0.99	Reference	
Inpatient	1816	0.95	1.06 (0.87-1.29)	.56
Complication				
No	366	0.75	Reference	
Yes	1156	0.90	1.24 (1.01-1.52)	.04
Duration (years)				
<5	1691	1.23	Reference	
≥5	1263	0.75	0.66 (0.56-0.79)	<.001
Baseline HbA_{1c} (%)				
7-8	298	0.61	Reference	
8-9	456	0.85	1.34 (1.04-1.72)	.03
9-10	381	0.85	1.30 (0.99-1.70)	.06
≥10	1253	1.28	1.72 (1.36-2.18)	<.001
FBG goal setting (mmol/L)				
≥6.1	2499	0.96	Reference	
<6.1	447	1.01	1.01 (0.80-1.27)	.95

[a]RR: relative risk.

[b]SMBG: self-monitoring blood glucose.

[c]N/A: not applicable.

[d]HbA_{1c}: hemoglobin A_{1c}.

[e]FBG: fasting blood glucose.

Table 7 shows the composite end points of patients reaching the target with no hypoglycemia events during a 3-month period. For HbA_{1c} <7% without SMBG ≤3.9 mmol/L at month 3, patients with complications (OR 0.68, 95% CI 0.54-0.84; *P*=.001) and those with a duration of diabetes for ≥5 years (OR 0.76, 95% CI 0.62-0.93; *P*=.008) had significantly lower odds of reaching the target with no hypoglycemia events. Furthermore, higher baseline HbA_{1c} levels in the ranges of 9%-10% (OR 1.26, 95% CI 1.03-1.55; *P*=.02) and ≥10% (OR 1.47, 95% CI 1.23-1.76; *P*<.001) were associated with increased odds of achieving the target. Also, those who set an FBG goal of <6.1 mmol/L at initiation had significantly higher odds of reaching the composite end point (OR 1.35, 95% CI 1.03-1.79; *P*=.03). None of these factors were related to the composite end points for achieving FBG <7 mmol/L without SMBG ≤3.9 mmol/L at month 3. Finally, for achieving FBG <6.1 mmol/L without SMBG ≤3.9 mmol/L at month 3, only the duration of diabetes for ≥5 years was associated with a significantly lower possibility of achieving this composite end point.

Table 7. Composite end points of patients reaching target with no hypoglycemia events during 3 months of TRIO monitoring in patients with self-monitoring blood glucose.

	Values, n	Month 3, n (%)	OR[a] (95% CI)	*P* value
HbA_{1c}[b] <7% without SMBG[c] ≤3.9 mmol/L				
All	5121	2055 (40.1)	N/A[d]	
Patient sources				
Outpatient	1987	750 (37.7)	Reference	
Inpatient	3134	1305 (41.6)	1.14 (0.92-1.41)	.23
Complication				
No	735	352 (47.9)	Reference	
Yes	1952	697 (35.7)	0.68 (0.54-0.84)	.001
Duration (years)				
<5	2325	1024 (44.0)	Reference	
≥5	2796	1031 (36.9)	0.76 (0.62-0.93)	.008
Baseline HbA_{1c} (%)				
7-8	942	436 (46.3)	Reference	
8-9	881	319 (36.2)	1.14 (0.94-1.38)	.20
9-10	811	297 (36.6)	1.26 (1.03-1.55)	.02
≥10	1495	579 (38.7)	1.47 (1.23-1.76)	<.001
FBG[e] goal setting, mmol/L				
≥6.1	4435	1735 (39.1)	Reference	
<6.1	686	320 (46.6)	1.35 (1.03-1.79)	.03
FBG <7 mmol/L without SMBG ≤3.9 mmol/L				
All	5988	2398 (40.0)	N/A	
Patient sources				
Outpatient	2203	883 (40.1)	Reference	
Inpatient	3785	1515 (40.0)	0.98 (0.81-1.18)	.80
Complication				
No	830	363 (43.7)	Reference	
Yes	2531	947 (37.4)	0.85 (0.7-1.04)	.11
Duration (years)				
<5	2831	1197 (42.3)	Reference	
≥5	3157	1201 (38.0)	0.93 (0.78-1.11)	.41
Baseline HbA_{1c} (%)				
7-8	957	438 (45.8)	Reference	
8-9	1005	436 (43.4)	1.08 (0.85-1.37)	.53
9-10	897	326 (36.3)	0.94 (0.73-1.20)	.61
≥10	2050	807 (39.4)	0.94 (0.75-1.17)	.58
FBG goal setting, mmol/L				
≥6.1	5071	1989 (39.2)	Reference	
<6.1	905	406 (44.9)	1.06 (0.84-1.33)	.62
FBG <6.1 mmol/L without SMBG ≤3.9 mmol/L				
All	5988	1174 (19.6)	N/A	

	Values, n	Month 3, n (%)	OR[a] (95% CI)	*P* value
Patient sources				
Outpatient	2203	438 (19.9)	Reference	
Inpatient	3785	736 (19.4)	0.83 (0.66-1.04)	.11
Complication				
No	830	194 (23.4)	Reference	
Yes	2531	434 (17.1)	0.81 (0.64-1.03)	.09
Duration (years)				
<5	2831	643 (22.7)	Reference	
≥5	3157	531 (16.8)	0.74 (0.59-0.92)	.007
Baseline HbA_{1c} (%)				
7-8	957	213 (22.3)	Reference	
8-9	1005	198 (19.7)	1 (0.75-1.34)	10
9-10	897	139 (15.5)	0.79 (0.58-1.09)	.15
≥10	2050	439 (21.4)	1.03 (0.79-1.36)	.82
FBG goal setting, mmol/L				
≥6.1	5071	955 (18.8)	Reference	
<6.1	905	218 (24.1)	0.97 (0.74-1.29)	.86

[a]OR: odds ratio.

[b]HbA_{1c}: hemoglobin A_{1c}.

[c]SMBG: self-monitoring blood glucose.

[d]N/A: not applicable.

[e]FBG: fasting blood glucose

Discussion

Principal Findings

The TRIO program, a large-scale health management initiative using a digital WeChat platform for patients with T2DM initiating BI treatment, demonstrated its effectiveness in improving glycemic control 3 months after initiating BI. Prior to enrollment in TRIO, patients with T2DM exhibited suboptimal blood glucose control, with elevated baseline HbA_{1c} (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 HbA_{1c} (–2.59%) and FBG (–2.77 mmol/L) were observed in the total population, accompanied by heightened proportions of achieving HbA_{1c} <7% (55.6%) and FBG target <7.0 mmol/L (61.3%) across diverse subgroups, such as patients from inpatient or outpatient care, patients with or with no complications, and patients with different length of diabetes duration, baseline HbA_{1c}, 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 with the traditional <7.0 mmol/L target. By setting a more rigorous FBG target of <6.1 mmol/L, better glycemic control was achieved without increased risk of hypoglycemia. These results hold promise for digital health tools such as TRIO in improving the overall management of T2DM in real-world clinical settings.

TRIO has shown effectiveness and safety in patients with T2DM 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 patients with 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 engagement among patients with prediabetes, showing a reduction of –0.33 mmol/L in HbA_{1c} levels over 3 years [15]. In our TRIO study, with a larger sample size, we achieved a greater HbA_{1c} reduction of –2.58 mmol/L. Furthermore, in a 12-week German trial involving individuals with type 2 diabetes on BI, a smartphone app (My Dose Coach) was compared with a written titration chart. The intervention group using the app exhibited a noteworthy reduction in HbA_{1c} levels compared with the control group (–0.31%; *P*=.04), with safety outcomes remaining unaffected. These findings suggest that app-assisted titration can enhance glycemic control in patients with type 2 diabetes who use BI [20].

TRIO has demonstrated that digital tools including health education and self-management modules added on BI might provide additional benefits to effectiveness in glycemic control than medication alone. The ORBIT study is an observational registry conducted in China with patients with T2DM who were inadequately controlled by OADs and initiated BI [21], with similar baseline HbA_{1c} (9.6%, SD 2%) but higher baseline FBG (11.7, SD 4.0 mmol/L) and shorter diabetes duration (6.4, SD

5.3 years) than those in our study. Notably, the change in HbA_{1c} 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 HbA_{1c} target of <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 (37,017/60,377, 61.3%) than those in the ORBIT study (2078/5571, 37.3%). Another significant study in this field, the First Basal Insulin Evaluation (FINE) Asia study, was a multinational, prospective, observational approach to assess BI's efficacy in patients with uncontrolled type 2 diabetes (HbA_{1c} ≥8%) [22].

In TRIO, baseline HbA_{1c} and FBG were as high as 9.6% and 9.5 mmol/L, respectively (Table 1), which suggests delayed initiation of BI. The American Diabetes Association and the European Association for the Study of Diabetes suggest that BI should be promptly considered after the apparent "failure" of lifestyle modifications, including diet and exercise in combination with metformin, particularly when HbA_{1c} levels remain at or exceed 7% for a span of 2-3 months [23]. However, consistent with our findings, delay in injectable therapies was universal [24,25]. Timely initiation of insulin such as BI after the failure of oral treatment is associated with better glycemic control [26].

Standard T2DM management advice recommends keeping HbA_{1c} 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 American Diabetes Association 2018 guidelines [28] or <6.1 mmol/L according to the American Association of Clinical Endocrinology-American College of Endocrinology and the International Diabetes Federation [29]. Previous studies support an FPG target of 6.1 mmol/L, showing better outcomes. Patients with FPG goals below 6.1 mmol/L had more significant HbA_{1c} 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 enrollment experienced both greater reductions in their HbA_{1c} levels (–2.64 vs –2.57%) and a higher HbA_{1c} target rate (67.8% vs 53.1%) than those with FPG goal setting ≥6.1 mmol/L (Tables 2 and 3). At the same time, hypoglycemic incidence and rate were comparable between the 2 groups. To enhance the management of hypoglycemic events, we recommend frequent SMBG monitoring, particularly during the initial weeks of insulin titration, to detect and address hypoglycemia promptly. Patient education on recognizing and treating hypoglycemic symptoms should be prioritized, alongside individualized insulin dose adjustments based on SMBG trends to minimize risk. Regular follow-ups are essential to reassess glycemic targets, such as FBG and HbA_{1c}, and to prevent overtreatment while maintaining optimal glycemic control. These measures can help balance achieving strict glycemic targets with ensuring patient safety.

Regarding the titration of BI 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 such as 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 36,037 patients with baseline and 3-month dosage data, 42.9% (15,444/36,037) of patients escalated their dosage during the program, while 7.1% (2546/36,037) maintained stability and 50.1% (18,047/36,037) of patients 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 in Multimedia Appendix 1) 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. First, a significant portion of patients lacked HbA_{1c} follow-up data at month 3, possibly introducing a compliance bias that could overstate TRIO's effectiveness by excluding those with less favorable HbA_{1c} reductions. Nonetheless, comparable baseline characteristics between compliant and noncompliant patients mitigate the risk of overestimation. Long-term data (months 3-12) are insufficient, leaving uncertainty about TRIO' s enduring effectiveness and ability to sustain patient adherence. Second, the judgment of hypoglycemia relied on SMBG, and the SMBG data were collected mainly through self-reporting on the WeChat platform, smart glucose devices, and regular phone calls by nurses, which may have a certain degree of deviation from the actual occurrence of hypoglycemia. Moreover, the absence of an RCT design and an external control group that included patients with type 2 diabetes who initiated only BI therapy without using TRIO may lead to the effect of TRIO to optimize glycemic control not solid enough. Therefore, it is necessary for future studies to design RCTs to evaluate the effectiveness and safety of intelligent blood glucose management in patients with diabetes with initiated BI therapy.

Conclusions

The TRIO program has demonstrated effectiveness in glycemic control, as reflected in HbA_{1c} and FBG levels, among patients with T2DM initiating BI therapy. The program has improved HbA_{1c} and FBG target rates and patient compliance with insulin treatments. 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 RCTs, is warranted to validate our study's findings and assess TRIO' s generalizability in real-world populations.

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Data Availability

The datasets generated during or analyzed during this study are not publicly available due to business confidentiality reasons but are available from the corresponding author upon reasonable request.

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.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Loss to follow-up, dosage regimen, fasting blood glucose (FBG) target rate, incidence of hypoglycemia, and levels of FBG during the TRIO optimal health management program.
[DOCX File , 51 KB-Multimedia Appendix 1]

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Abbreviations

BI: basal insulin
FBG: fasting blood glucose
FPG: fasting plasma glucose
HbA_{1c}: hemoglobin A1c
LS: least square
OAD: oral antidiabetic drug
OR: odds ratio
PPG: postprandial glucose
RCT: randomized controlled trial
RR: relative risk
SMBG: self-monitoring blood glucose
T2DM: type 2 diabetes mellitus

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