Title: An observational study to evaluate the effectiveness of physician-targeted education for improving glycemic management of patients with type 2 diabetes mellitus (BEYOND II)

Running title: Optimizing glycemic management in type 2 diabetes

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ABSTRACT

Background: As there has been no quality improvement initiatives targeting patients with type 2 diabetes mellitus (T2DM) receiving basal insulin therapy, this study evaluated the effectiveness of physician-targeted education for optimizing glycemic management in these patients in China.

Methods: This multicenter, open-label, observational study conducted across China had a baseline sample survey, followed by a 6-month education program, and ended with a post-education sample survey. Education based on T2DM treatment guidelines was given at month 1 and 3, and was reinforced by self-audit every month. Each hospital enrolled 100 patients with T2DM receiving basal insulin at both baseline and post-education survey. The primary outcome was the proportion of hospitals meeting individual improvement goals. The goal setting was based on proportion of patients achieving HbA1c <7.0% in each hospital at baseline survey.

Results: Overall, individual improvement goal was achieved by 35 (49%) centers. Hospitals with poor glycemic management at baseline survey had higher possibility to improve after 6-month education. Two large sample survey at baseline and post-education periods showed improved glucose management among these hospitals. Higher proportion of patients achieved

HbA1c <7.0% in post-education survey (27.2 vs. 36.5%; p<0.001) with reduced HbA1c levels (8.10% vs. 7.72%; p<0.001]). Questionnaires from 723 physicians showed that confidence and practice of basal insulin use were significantly improved.

Conclusions: Physician-targeted education improved glycemic management of patients with T2DM in 71 hospitals of China and was more effective at hospitals with poor glycemic management at baseline survey.

Study Registration: Chinese Clinical Trials registry, ChiCTR-OOC-15006935

HIGHLIGHTS

- This study investigated if physician-targeted education can improve outcomes in Chinese patients with type 2 diabetes mellitus receiving basal insulin therapy.
- The 6-month education program improved glycemic management in approximately50% of the participating hospitals. More patients achieved acylated hemoglobin <7% at post-education sample survey than at the baseline sample survey.
- Physician-targeted education was more effective at hospitals that had poor glycemic management at baseline sample survey.

Key words: Type 2 diabetes mellitus, Basal insulin, Education, Physician, Glycemic management

INTRODUCTION

A worldwide diabetes epidemic continues to unfold; according to the International Diabetes Federation, in 2017, there were 425 million people affected by diabetes worldwide, and the majority of them had type 2 diabetes mellitus (T2DM).[1] Due to the progressive nature of T2DM, the majority of patients will eventually require insulin therapy.[2,3] Both international and Chinese treatment guidelines recommend the initiation of basal insulin (BI) for patients unable to achieve glycemic targets with 1–2 oral antidiabetic drugs (OADs).[4–6]

Despite the recommendations of evidence-based guidelines, large gaps exist globally in the achievement of glycemic control for patients with T2DM receiving BI in clinical practice.[7–9] For example, a retrospective analysis using data from a US claims database indicated that the proportion of patients achieving HbA1c <7.0% (53 mmol/mol) was similar for BI users at baseline (26%) and at 3 months follow-up (27%).[10] Furthermore, the large Observational Registry of Basal Insulin Treatment (ORBIT) study found that BI was initiated relatively late with average glycated hemoglobin (HbA1c) of 9.6% (81 mmol/mol).[11] Another multicenter, cross-sectional survey conducted in China revealed that out of 80,973 patients treated by BI plus OAD(s), only 26.21% achieved HbA1c <7% (53 mmol/mol).[12] Thus, achieving and maintaining glycemic control in patients receiving BI therapy is a global challenge.

In China, the China Guideline for Type 2 Diabetes is enforced by Chinese Diabetes Society (CDS) through creating awareness and knowledge exchange.[6] Though, the awareness and implementation of evidence-based T2DM treatment guidelines varies across China in different geographical regions, hospital grades, professional statuses and specialties. Reportedly, less than

30% of physicians completely understand the guidelines and apply them in practice.[13] For several decades, quality improvement interventions directed at patients, doctors, and health systems have aimed to address gaps in the management of T2DM not fully addressed through new therapeutics or devices.[14,15] Results from a large meta-analysis showed that predefined quality improvement strategies led to improvements in glycemic control.[14]

However, to the authors' knowledge, there have been no previous quality improvement initiatives that focused on patients already receiving BI therapy,[16–18] whose glycemic control is typically relatively poor.[10–12] Furthermore, while both nurses and patients play an important role in quality improvement initiatives, physicians are particularly key in adopting guidelines and improving glycemic control for patients receiving insulin.[19–21] The BEYOND II study aimed to evaluate the effectiveness of physician-targeted education for improving management in T2DM patients receiving BI therapy.

MATERIALS AND METHODS

Study design

BEYOND II was a multicenter, open-label, observational study conducted at study centers across China from October 2015 to March 2017 (Supplementary Table 1). The study consisted of a baseline sample survey to evaluate the glucose control in the hospital before education, followed by a 6-month physician-targeted education program, and ended with a post-education sample survey to evaluate the glucose control in the hospital after education (Supplementary Figure 1). During both survey periods, physicians at each study site were mandatorily required to consecutively enroll around 100 individuals (200 in total) with T2DM receiving BI, and collect

laboratory test results from routine practice. The patients enrolled at post-educational survey were allowed to be different from those enrolled in the baseline survey. To reduce selection bias, all data were collected within 2 months of recruitment of the first patient at each center, and recorded in an electronic Case Report Form (e-CRF). Participating physicians' confidence and daily practice in BI treatment were also assessed at baseline and post-education by questionnaire.

The study protocol was approved by the Clinical Trial Ethics Committee of the Third Affiliated Hospital, Sun Yat-sen University (Reference Number [2015] 2-152 on 21 July 2015). The study was conducted in accordance with the Declaration of Helsinki and in-line with The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use guidelines for Good Clinical Practice (GCP) and Chinese GCP. Written, informed consent was obtained from each study participant. This study was registered in the Chinese Clinical Trials registry: ChiCTR-OOC-15006935.

Study center and physician selection criteria

Endocrinology departments at Tier 3, Tier 2 or county-level hospitals across China with a head of department willing to support the implementation of the education and adopt a standard T2DM treatment pathway were eligible for inclusion in this study. The majority of T2DM cases in China are treated at Tier 2 and 3 hospitals; therefore, eligible study centers represented the standard of care in China.

Heads of enrolled endocrinology departments conferred with departmental physicians and nominated participants. An inclusion target of ≥60% of outpatient endocrinologists at each study

center was set to provide a representative sample of the overall treatment quality. Participating physicians were required to complete the whole study process, and replacement of physicians during the study was not allowed.

Patient inclusion criteria

Adults (≥18 years) with T2DM who had received BI-based therapy as outpatients for ≥3 months were eligible for inclusion. Study subjects were followed-up for ≥3 months prior to enrolment at the respective study center, with HbA1c and fasting plasma glucose (FPG) measurements available 1 month before entering the study. Since this was an observational study, no medication was provided by the sponsor. The use of OADs and prandial insulin, and BI dose, were chosen at investigators' discretion in-line with treatment guidelines and local label indications.

Education and Study Committee

Physician education was based on a standard T2DM treatment pathway and also incorporated self-audit and regular peer-to-peer discussion. The treatment pathway followed CDS 2013 (Supplementary Figure 2) and American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) 2013 (Supplementary Figure 3) guidelines.[6,22] Training covered offering advice on diet, smoking cessation, daily physical activity and maintenance of a healthy weight, as well as information about insulin preparations, correct dosing, when and how to administer insulin, self-monitoring blood glucose and management and prevention of hypoglycemia.

Participating physicians attended an initial face-to-face interactive training workshop provided by the Study Committee. Participants then applied the standard T2DM treatment pathway, insulin initiation/titration scheme and appropriate patient education in outpatient practice for 6 months. During the 6-month practice, regular self-audit about implementation of standard insulin treatment pathway was also done every month. All the participating investigators were required to attend the monthly meeting to discuss any issue of BI management during daily practice, share valuable experiences, and come to potential solutions after peer-to-peer discussion. The principal investigator was responsible for self-audit in the study center.

Objectives and evaluation criteria

The primary endpoints of BEYOND II was the percentage of hospitals meeting individual improvement goals. The goal setting was based on proportion of patients achieving HbA1c <7.0% (53 mmol/mol) in each hospital at baseline sample survey. The Study Committee member and principle investigator of each study center discussed the baseline data and aligned an appropriate improvement goal for each center, accounting for relevant factors such as patient characteristics and available resources.[23]

Secondary endpoints included assessment of glycemic control and safety in the baseline and post-education surveys, as indicated by mean HbA1c and FPG, proportion of patients achieving HbA1c <7% and FPG <6.1 mmol/L, and frequency of hypoglycemic events (blood glucose ≤3.9 mmol/L) and severe hypoglycemic events (hypoglycemic episodes requiring the assistance of another person or admission to hospital) in the 2 weeks before enrolment. Physicians' confidence

and daily practice in BI treatment were assessed by questionnaire (Supplementary Figures 4 and 5).

Exploratory objectives included investigation of the relationship between hospital characteristics at baseline survey and absolute and relative improvement of hospital at post-education survey.

Statistical methods

The primary statistical objective is to estimate the percentage of hospitals meeting individual improvement goals which would be provided along with the corresponding 95 confidence interval. A sample size of 150 Tier 2 and 3 hospitals was calculated to allow estimation of the two-sided 95% confidence interval (CI) for the rate of hospitals that met improvement goals with a precision of approximately ±8.3%, assuming 50% of hospitals would meet improvement goals (the five county-level hospitals were included in an exploratory group; data from these hospitals will be assessed separately).

A sample size of approximately 100 subjects per cohort in each study center was calculated to allow estimation of the two-sided 95% CI for the proportion of subjects achieving HbA1c <7% (53 mmol/mol) with a precision of approximately ±10%, assuming 50% of patients would achieve HbA1c <7% (53 mmol/mol). An HbA1c of <7% (53 mmol/mol) was chosen in the sample size estimation, as this was used to set improvement goals for all study centers.

Continuous variables were summarized with descriptive statistics as N, N miss (number of missing values), mean, standard deviation (SD), minimum, median and maximum. Major continuous variables included average HbA1c and average FPG. We assumed that large sample

size and normal distribution of data will be applied. A two sample t-test was used to compare baseline and post-educational (6-month) data for the continuous variables.

Discrete variables were summarized in frequency tables (N, %). Major discrete variables included percentage of patients achieving glucose goal (HbA1c <7%), percentage of patients with FPG achieving goal (<6.1 mmol/L), hypoglycemia rate, and severe hypoglycemia rate. The chi-square test was used to test the comparison of baseline and post-educational (6-month) data. Univariate and multivariate regression analysis were used to assess factors influencing hospitals' absolute and relative improvements in glycemic management. The factors included in the univariate analysis were proportion of patients achieving HbA1c <7% at baseline survey (top 50% vs. bottom 50%), region of China (South vs. North), hospital level (tertiary general hospital vs. secondary general hospital), affiliated teaching hospital of medical university (yes vs. no). The stepwise method was used to select the risk factors in multivariate analysis.

Values for missing data were not imputed unless otherwise stated.

RESULTS

Primary endpoint

A total of 73 Tier 2 and 3 hospitals entered into the study and 71 completed the post-education patient enrolment. Of the 71 hospitals that competed the study, 63 were Tier 3 and 8 were Tier 2; 34 were located in North China and 37 in South China, and 26 were affiliated to a medical university. At baseline survey, the proportion of patients achieving HbA1c <7% (53 mmol/mol) was <20% at 11 hospitals, 20-35% at 47 hospitals, and ≥35% at 13 hospitals. At post-education

survey, the proportion of patients achieving HbA1c <7% (53 mmol/mol) was <20% at 5 hospitals, 20-35% at 30 hospitals, and ≥35% at 36 hospitals.

The primary endpoint was achieved by 35/71 (49.3%, 95% CI: 37.2 to 61.4%) hospitals. The number of hospitals with >0% absolute improvement in the proportion of patients achieving HbA1c <7% (53 mmol/mol) was 58/71 (81.7%), of which 41 (70.7%) achieved an improvement of >5% (Supplementary Table 2). Detailed improvement data for each hospital are provided in Supplementary Table 3.

Factors related to hospitals improvement (n=71)

A total of 71 hospitals were included in an analysis of the relationship between hospital characteristics at baseline sample survey and absolute or relative improvement at post-education sample survey. The definition of improvement was based on change of proportion of patients achieving HbA1c<7% between baseline and post-education sample survey in the participating hospitals. The distribution of hospitals by absolute improvement (no improvement, ≤10% and >10%) differed significantly between the top 50% versus bottom 50% of hospitals stratified by proportion of patients achieving HbA1c <7% at baseline survey. A similar difference was observed between hospitals affiliated to medical universities or not. In contrast, no difference in distribution was observed according to region or hospital Tier (Table 1). Similar results were observed for relative improvement (no improvement, ≤10% and >30%) (Table 1).

A multivariate analysis revealed that only the variable 'hospitals stratified by proportion of patients achieving HbA1c <7% at baseline survey (top 50% vs. bottom 50%)' was significantly

negatively associated with absolute (odds ratio [OR] = 0.33 [95% CI, 0.13 to 0.83]; p=0.018) or relative improvement (OR = 0.25 [95%, 0.10 to 0.64]; p=0.004) (Table 2). No association was found between hospital region, hospital level, or affiliation status with medical universities.

Patients profile at baseline and post-education sample survey (n=6386 and 6353)

A total of 6561 patients were enrolled in the baseline sample survey, with 6386 evaluable patients. Following the education program, 6413 patients were enrolled into the post-education sample survey, with 6353 evaluable patients. Overall, the demographics of patients in the baseline and post-education survey were comparable, with a similar mean age, body mass index (BMI), duration of T2DM, prevalence of diabetic complications and average daily BI dose (Supplementary Table 4).

Overall, in the post-education sample survey, patients' glycemic control was improved compared to baseline sample survey (Table 3). Compared with baseline, patients enrolled in the post-education survey had a lower mean HbA1c level (8.10% ± 1.73% [65 mmol/mol] vs. 7.72% ± 1.58% [61 mmol/mol]; p<0.001) and a higher proportion achieved HbA1c <7% (53 mmol/mol) (27.2 vs. 36.5%; p<0.001). Similarly, compared with baseline survey, patients in the post-education survey had a lower mean FPG (9.10 vs. 8.44 mmol/L; p<0.001) and a greater proportion achieved FPG <6.1 and <7.0 mmol/L (15.6 vs. 19.6%; p<0.001 and 29.5 vs. 37.2%; p<0.001). Finally, the rate of hypoglycemia was lower in the post-education survey, although this did not reach statistical significance (4.4 vs. 3.8%; p=0.077).

At hospitals that met individualized improvement targets, compared with baseline, the proportion of patients in the post-education survey achieving HbA1c <7% (53 mmol/mol) was significantly higher (25.6 vs. 43.1%; p<0.001), mean HbA1c and FPG levels were significantly lower (8.10% [65 mmol/mol] vs. 7.46% [58 mmol/mol]; p<0.001, and 9.02 vs. 8.04 mmol/L; p<0.001) (Supplementary Table 5). In contrast, at hospitals not meeting targets, the proportion of patients in the baseline and post-education surveys achieving HbA1c <7% (53 mmol/mol) was similar (29.1 vs. 29.8%; p=0.537), and differences in mean HbA1c and FPG levels were lower in magnitude (8.08 [61 mmol/mol] vs. 7.99% [64 mmol/mol]; p=0.045 and 9.15 vs. 8.85 mmol/L; p<0.001).

Physician questionnaire analysis (n=723)

In total, 793 physicians were included at baseline, of whom 764 took part in the 6-month education and 723 had evaluable data. According to the baseline survey, 550 (76.1%) physicians self-reported 'confidence in most cases' in initiating BI therapy; this number increased to 602 (83.3%, p=0.002) at post-education survey (Figure 1A). Similarly, the number of physicians reporting 'confidence in most cases' in management of hypoglycemia also increased between baseline and post-education (569 [78.7%] vs. 607 [84.0%]; p=0.007) (Figure 1G). However, there was no statistically significant difference in the proportion of physicians 'confident in most cases' about reaching FPG goals via BI titration between baseline and post-education (80.2% vs. 82.6%, p=0.076) (Figure 1D). A subgroup analysis revealed that at study centers meeting individualized improvement targets had significant changes in treatment confidence (Figure1B,

1E, 1H), compared no significant changes in centers not meeting the improvement targets (Figure 1C, 1F, 1I).

A survey of daily insulin treatment practice revealed that the proportion of physicians who 'always' (100% of the time) or 'usually' (80-99% of the time) prescribed BI as initial treatment and titrated BI dose to achieve FPG <6.1mmol/L was higher at post-education survey compared with baseline survey (Figure 2A, 2D). Furthermore, the proportion of physicians who 'always' or 'usually' replaced BI with premixed insulin showed a small decrease post-education versus baseline (Figure 2G). The initiation of BI for individuals not achieving HbA1c and FPG targets was largely comparable at baseline and post-education (Figure 2J). In addition, physicians at study centers that met improvement targets showed more marked changes in clinical practice in terms of BI use following the education (Figures 2B, 2E, 2H, 2K). At centers not meeting targets there was no significant change in clinical practice (Figures 2C, 2F, 2I, 2L).

DISCUSSION

There is currently a global need to improve rates of glycemic control among patients with T2DM receiving BI-based treatment.[10–12] To the authors' knowledge, BEYOND II is the first study to demonstrate the effectiveness of physician-targeted education for improving glycemic management of patients with T2DM receiving BI. Primary endpoint revealed that the 6-month education program led to achievement of individualized improvement goals at around 50% of hospitals. The primary endpoint was further supported by the finding that the proportion of patients achieved HbA1c<7% at post-education sample survey was higher than at baseline sample survey. Furthermore, multivariate analysis revealed that hospitals with poor glycemic

control at baseline survey had higher possibility to improve after 6-month education; the results indicate that physician-targeted education may be more effective at hospitals with poor glycemic management at baseline survey.

The primary objective of this study was to observe the change in the glucose management of physicians and hospital after education. Two sample surveys were the best strategy to meet this objective. During the 6-month education period, physicians applied the standard treatment procedures recommended in training, which might have improved their glucose management and benefit all the patients treated by them. Following-up the same 100 patients would only observe the change in HbA1c of these patients. To ensure all the enrolled patients were impacted by education, only patients who were being followed-up at the study at site and receiving BI therapy for $\geq$ 3 months were included. Thus, the patients received treatment from the trained physicians for at least 3 months before post-education survey.

One unique strength of BEYOND II study is to use individualized improvement goals as primary endpoint. The use of individualized goals would provide physicians with a clear overview of glycemic control at their hospital and give them a tangible improvement goals to achieve. In contrast, all previous quality improvement studies used HbA1c reductions in overall patients as primary endpoint.[10–12,14,18] Another important strength of this study was the incorporation of multiple elements in the physician-targeted education including the use of evidence-based guidelines and training on how to educate patient, both of which have been shown to be effective in improving diabetes care.[14,18] Moreover, the implementation of regular peer-to-peer review and discussion are suggested as particularly useful in stimulating changes in physicians' habits.[24–26]

Finally, this study included self-assessment of physicians' confidence and clinical practice in BI use by questionnaire. These questionnaires enabled investigation of the relationship between physicians' self-assessed confidence, their behavior in real clinical practice, and the outcomes of diabetes care at their hospitals. The final results demonstrated that physicians' confidence and behavior change was positively associated with the improvements in glycemic control at their hospitals.

However, BEYOND II study may have limitations. Firstly, the lack of a control group did not allow direct comparison of the education versus no education or an alternative education. Secondly, two separate groups of patients were enrolled at the baseline and post-education surveys which may have resulted in selection bias. To reduce the selection bias of the two surveys, a consecutive 2-month enrollment was adopted. A longer enrollment duration (3-5 month) would have given physicians a chance to select patients with better glycemic control to meet their post-education target. However, we acknowledge that the selection bias could not be totally avoided in this study. Thirdly, the post-education survey was conducted right after the 6-month education. We acknowledge that if there was another 2-month survey after 1-year completion of this study, it would have ensured that the impact is sustainable. Lastly, the findings could have been influenced by Hawthorne effect as the physicians were aware of being under observation. [27] However, a previous study reported limited influence of the Hawthorne effect on patient-physicians visits, except for the subgroup of vulnerable patients, where it slightly affected the observations.[28]

In conclusion, physician-targeted education improved glycemic management of Chinese patients with T2DM in 71 hospitals of China and appeared to be more effective at hospitals with poor average glycemic control at baseline. However, future studies are warranted to confirm the program's effectiveness (e.g. using control groups) and to establish the effectiveness of physicians' education in the whole country.

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Tianhong Luo and Nancy Cui were responsible for the design of the study, collecting and managing data, and interpretation of data. Jianping Weng participated in study concept and design, data analysis, interpretation of data, and critical revision of the manuscript for important intellectual content. All other authors participated in the data analysis and manuscript composing. All authors have read and approved the final version of the manuscript for submission.

DISCLOSURES

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DATA ACCESSIBILITY

Qualified researchers may request access to patient level data and related study documents including the clinical study report, study protocol with any amendments, blank Case Report Form, statistical analysis plan, and dataset specifications. Patient level data will be anonymized and study documents will be redacted to protect the privacy of our trial participants. Further

details on Sanofi's data sharing criteria, eligible studies, and process for requesting access can be found at: https://www.clinicalstudydatarequest.com/.

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FIGURE LEGENDS

Figure 1. Results of physician (n=723) confidence in basal insulin use assessed by questionnaire for all study centers (A, D, G), those which achieved individualized improvement targets (n=356; B, E, H) and those which did not (n=367; C, F, I). FPG, fasting plasma glucose.

Figure 2. Physician (n=723) clinical practice in basal insulin use assessed by questionnaire for all study centers (A, D, G, J) for those which achieved individualized improvement targets (n=356; B, E, H, K) and those which did not (n=367; C, F, I, L). FPG, fasting plasma glucose.

TABLES

Table 1. Distribution of hospitals by absolute and relative improvement

Hospital characteristics at baseline survey	Hospitals by absolute improvement				Hospitals by relative improvement			
	No improvement (n†=13)	≤10% (n†=23)	>10% (n†=35)	P-value‡	No improvement (n†=13)	≤30% (n†=24)	>30% (n†=34)	P-value‡
Proportion of patients achieving HbA1c <7% at baseline survey, n† (%)				0.047				0.013
Top 50%	10 (76.9)	12 (52.2)	13 (37.1)		10 (76.9)	14 (58.3)	11 (32.4)	
Bottom 50%	3 (23.1)	11 (47.8)	22 (62.9)		3 (23.1)	10 (41.7)	23 (67.6)	
Region of China, n† (%)				0.523				0.382
South	7 (53.8)	14 (60.9)	16 (45.7)		7 (53.8)	15 (62.5)	15 (44.1)	
North	6 (46.2)	9 (39.1)	19 (54.3)		6 (46.2)	9 (37.5)	19 (55.9)	
Hospital level, n† (%)				0.222				0.198
Tertiary general hospital	13 (100.0)	21 (91.3)	29 (82.9)		13 (100.0)	22 (91.7)	28 (82.4)	
Secondary general hospital	0	2 (8.7)	6 (17.1)		0	2 (8.3)	6 (17.6)	
Affiliated to medical university, n† (%)				0.002				0.003
Yes	10 (76.9)	4 (17.4)	12 (34.3)		10 (76.9)	5 (20.8)	11 (32.4)	
No	3 (23.1)	19 (82.6)	23 (65.7)		3 (23.1)	19 (79.2)	23 (67.6)	

†Number of hospitals; ‡Chi-squared test

Table 2. Logistic regression analysis of factors associated with hospitals' absolute and relative improvements

	Univariate analysis			Multivariate analysis		
	Odds ratio	**95% CI**	**p-value**	**Odds ratio**	**95% CI**	**p-value**
Factors associated with absolute improvement						
Proportion of patients achieving HbA1c <7% at baseline survey (top 50% vs. bottom 50%)	0.33	(0.13, 0.83)	0.018	0.33	(0.13, 0.83)	0.018
Region of China (South vs. North)	0.67	(0.28, 1.63)	0.382			
Hospital level (tertiary general hospital vs. secondary general hospital)	0.26	(0.05, 1.40)	0.116			
Affiliated to medical university (yes vs. no)	0.46	(0.18, 1.14)	0.095			
Factors associated with relative improvement						
Proportion of patients achieving HbA1c <7% at baseline survey (top 50% vs. bottom 50%)	0.25	(0.10, 0.64)	0.004	0.25	(0.10, 0.64)	0.004
Region of China (South vs. North)	0.62	(0.26, 1.51)	0.294			
Hospital level (tertiary general hospital vs. secondary general hospital)	0.24	(0.04, 1.32)	0.101			

Affiliated to medical university (yes vs. no)	0.40	(0.16, 1.01)	0.052

In multivariate analysis, the stepwise method was used to select the risk factors from univariate analysis.

Table 3. Summary of glucose management at baseline and post-education sample survey

Variable[†]	**Baseline sample survey (n=6386)**	**Post-education sample survey (n=6353)**	**Difference (95% CI)**	**P-value**[‡]
HbA1c, %	8.10 (1.732)	7.72 (1.579)	-0.38 (-0.43 to -0.32)	<0.001
HbA1c <7%, % (n)	27.2 (1740)	36.5 (2322)	9.3% (7.7% to 10.9%)	<0.001
Adjusted HbA1c target[§], % (n)	34.2 (2183)	43.2 (2743)	9.0% (7.3% to 10.7%)	<0.001
FPG, mmol/L	9.10 (3.580)	8.44 (3.172)	-0.66 (-0.78 to 0.54)	<0.001
FPG <6.1mmol/L, % (n)	15.6 (994)	19.6 (1247)	4.1% (2.7% to 5.4%)	<0.001
FPG <7.0 mmol/L, % (n)	29.5 (1883)	37.2 (2363)	7.7% (6.1% to 9.3%)	<0.001
Incidence of hypoglycemia, % (n)	4.4 (282)	3.8 (241)	-0.6 (-1.3% to 0.1%)	0.077

[†]Values are mean (standard deviation) unless otherwise specified; [‡]Chi-squared test for categorical variables and Student's t-test for continuous variables; [§]adjusted HbA1c target calculated using an adjusted HbA1c target of ≤7.5% (58 mmol/mol) for patients with existing cardiovascular disease or aged ≥65 years. FPG, fasting plasma glucose; HbA1c, glycated hemoglobin.