

Title: Does a patient-managed insulin intensification strategy with insulin glargine and insulin glulisine provide similar glycemic control as a physician-managed strategy? Results of the START (Self-Titration with Apidra® to Reach Target) Study – A randomized non-inferiority trial

Short Running Title: Patient-managed insulin intensification

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Abstract

Objective: Diabetes self-management is universally regarded as a foundation of diabetes care.

We determined whether comparable glycemic control could be achieved by self-titration versus physician titration of a once-daily bolus insulin dose in patients with type 2 diabetes unable to achieve optimal glycemia control with a basal insulin.

Research Design and Methods: Patients with type 2 diabetes, a HbA1c above 7% (53 mmol/mol) and with either nocturnal hypoglycemia episodes or on sufficient basal insulin glargine (\pm oral agents) to achieve a fasting plasma glucose \leq 6 mmol/L (108 mg/dL) were studied. Participants all had bolus insulin glulisine added at breakfast and were allocated to either algorithm-guided patient self-titration versus physician titration. The primary outcome was HbA1c \leq 7% (53 mmol/mol) without severe hypoglycemia.

Results: After a mean (SD) follow-up of 159.4 days (36.2), 28.4% of participants in the self-titration arm versus 21.2% in the physician titration arm achieved HbA1c \leq 7% (53 mmol/mol) without severe hypoglycemia (between-group absolute difference = 7.2%; 95% CI: -3.2 to 17.7). The lower end of this 95% composite interval was within the predetermined noninferiority boundary of -5% (p noninferiority=0.011).

Conclusions: In patients with type 2 diabetes on stable doses of basal insulin glargine who require bolus insulin, a simple bolus insulin patient-driven titration algorithm is as effective as a physician-driven algorithm.

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Key words: type 2 diabetes mellitus, HbA_{1C}, basal-plus/basal-bolus insulin strategy, patient-driven, primary care

Due to the progressive nature of type 2 diabetes mellitus, exogenous insulin is often required to sustain optimal metabolic control.(1) This is a particular challenge in the primary care setting where over 90% of patients with type 2 diabetes are managed (2) and where there is a lack of confidence and skill in insulin intensification strategies.(3) Basal insulin analogues are often added to oral antihyperglycemic agents (OADs) (4, 5)with a number of successfully tested algorithms for initiation and titration.(6-9) Indeed, these patient-driven basal insulin algorithms have been demonstrated to be safe, efficacious to improve glycemic control (6, 7) and successfully implemented in the primary care practice setting.(10)

Over time, basal insulin may be insufficient to maintain optimal glycemia control in patients with type 2 diabetes due a rise of post-prandial glucose levels despite normal fasting glucose levels. Hence, to achieve glycemic targets, treatment of type 2 diabetes may have to progress beyond basal insulin. As HbA_{1C} reflects the contribution of both fasting plasma glucose (FPG) and postprandial plasma glucose (PPG), optimal insulin therapy should focus on both FPG and PPG.(11-18) Elevated FPG is often targeted first with basal insulin, while elevated PPG indicates the need for bolus insulin. (19) Thus the addition of bolus insulin has been recommended when HbA_{1c} levels remain above target despite achieving an acceptable fasting plasma glucose with basal insulin.(20)

There has been increasing acceptance of a strategy that progressively adds bolus to basal insulin.

(21-24) However, the optimal way to do this is not clear. It is also unclear whether a patient driven self-titration algorithm would achieve glycemic control that was comparable to that achieved by physician-titrated preprandial insulin. This question was assessed in the START (Self-Titration with Apidra® to Reach Target) randomized controlled trial.

RESEARCH DESIGN AND METHODS

START was a randomized, parallel group, open label, stratified multicenter clinical trial designed to determine whether patient self-titration of a preprandial insulin dose was non-inferior to physician titration in people with type 2 diabetes unable to achieve optimal glycemia control with a basal insulin. A non-inferiority design was chosen to determine whether a patient-managed basal-plus insulin titration algorithm was similar to a physician-managed basal-plus insulin titration algorithm in patients with poorly controlled type 2 diabetes.

This trial was conducted in 47 primary care sites from across Canada. Volunteer patients with type 2 diabetes (age ≥ 30 years) were recruited at each site. Patients were eligible to enter the 12 week run-in phase if they were treated for at least 3 months and either (a) were on basal insulin (insulin glargine, NPH, or insulin detemir) as their only insulin with or without OADs and had an $HbA_{1C} > 7.0\%$ (53 mmol/mol), or (b) were insulin naïve but taking 2 or 3 OADs and had a $HbA_{1C} \geq 7.8\%$ (62 mmol/mol).

During the run-in phase, patients either began or self-titrated bedtime insulin glargine (glargine)

doses using the INSIGHT protocol [i.e. increasing by 1 U/day until the pre-breakfast capillary glucose value was ≤ 5.5 mmol/L (99 mg/dL)]. (6) Patients not taking insulin at baseline started glargine at 10 units/day; (6) patients on glargine were started on their existing dose; patients on once daily NPH switched to the same dose of glargine; patients on twice daily NPH started glargine at 80% of the total daily NPH dose (but not less than 10 units per day); patients on once or twice daily insulin detemir started glargine at 70% of the total daily insulin detemir dose (but not less than 10 units per day).

Patients entered the 24 week randomized treatment phase if their HbA_{1C} levels remained $>7.0\%$ (53 mmol/mol) and they had either a) ≥ 1 episode(s) of confirmed nocturnal hypoglycemia (blood glucose < 4.0 mmol/L (72 mg/dL); or b) ≥ 2 measurements of FPG ≤ 6.0 mmol/L (108 mg/dL) within the previous week (i.e. there was no “glycemic room” to continue glargine up-titration). At each site, patients were randomized 1:1 to either the patient-managed or physician-managed titration algorithms using concealed allocation. Randomization was stratified by site and previous basal insulin use.

Intervention

Following randomization, all patients continued on their fixed glargine dose and added insulin glulisine (glulisine) before breakfast. Patients were instructed to eat their usual breakfast and were not required to log their diet. Breakfast was chosen to 1) maximize patient safety to reduce the risk of nocturnal hypoglycemia; 2) expand on the common practice that many patients on a basal insulin routinely test their

blood glucose in the morning and the addition of a breakfast prandial insulin self-titration algorithm requires only one extra self-monitoring test later in the same morning; 3) patient convenience of injecting at home; 4) optimizing blood glucose earlier in the day may help maintain good glycemic control for the remainder of the day; 5) easier for patients to pursue sequentially with the same dosage titration algorithm to adjust for injection at subsequent meals in their future care.

Those randomized to the patient-managed arm received a pamphlet explaining the self-titration method. The starting dose of glulisine was 2 U and they were instructed to self-titrate 1 U/day to reach a target 2-hour PPG level between 5.0 and 8.0 mmol/L (90 and 144 mg/dL). The PPG was measured 2 hours after the start of breakfast. Once the target was attained, the maintenance dose was based on the monitoring of 2 or 3 2-hour PPGs per week.

Those randomized to the physician-managed arm had a starting dose of insulin glulisine of 2U recommended to the physicians but this dose, and the titration and self-monitoring of blood glucose monitoring (SMBG) schedules, were left to the physicians' discretion. Patients in this arm were required to contact their physician prior to any dose adjustment.

Primary and Secondary Outcome Measures

The primary outcome was the achievement of a HbA_{1c} $\leq 7\%$ (53 mmol/mol) without severe hypoglycemia 24 weeks after randomization. Secondary outcome measures included changes in HbA_{1c}, FPG, 7-point blood glucose profile (fasting before breakfast, 2 hours after breakfast,

before lunch, 2 hours after lunch, before dinner, 2 hours after dinner, at bedtime), and body weight from randomization to end point. Blood glucose levels and the 7-point blood glucose profile were measured by patients using a SMBG system (FreeStyle Lite™ blood glucose meter plus test strips; Abbott). The change between FPG and 2hr PPG and the total area under the 7-point glucose profile curve were calculated.

Hypoglycemic and adverse events were monitored for safety. All hypoglycemic episodes were recorded and were deemed confirmed if accompanied by a documented glucose value.

Annualized rates for hypoglycemia were calculated for those who had any hypoglycemic events as the total number of episodes/total patient-years. Nocturnal and severe (required assistance and FPG <2.0 or responded to counteractive treatment) episodes were noted.

Other secondary outcome measures included the dose of glulisine and health resource utilization (numbers of blood glucose test strips used, office visits and telephone calls to physician).

Patient satisfaction with treatment was assessed with the Diabetes Treatment Satisfaction Questionnaire (DTSQc – 8-item questionnaire scored from -3 to +3). (25) Physician satisfaction with the two insulin titration algorithms was assessed at the study end with a brief 7-question survey using a 7 point Likert scale scored from +3 to -3 refer to the Appendix.

Statistical methods

Intent-to-treat (ITT) analysis was performed on the primary outcome for all randomized patients.

The primary outcome, the proportion calculated with patients meeting the end criteria ($HbA_{1C} \leq 7.0\%$ (53 mmol/mol) with no severe hypoglycemia) in the numerator and all patients randomized to that group in the denominator. Patients missing endpoint data were assumed not to meet it.

The sample size of 320 randomized patients (160 patients for each titration algorithm) was based on an expected 10% difference between titration algorithms for the primary outcome with an 80% power and a non-clinically significant difference/margin of 5%.

To define non-inferiority, the 95% confidence interval (CI) of the difference between treatment algorithms was examined and if the lower end of the CI was $\geq -5.0\%$ the patient-managed arm was deemed non-inferior to the physician-managed arm. The non-inferiority boundary of $\geq -5.0\%$ was based upon the clinically important absolute difference of 10%; one half of this absolute difference was selected as the boundary. A test for the significance of the non-inferiority was performed.

Secondary outcome analyses were performed for a modified ITT population. This population included all randomized patients treated with glulisine who had results for visits at 12 weeks or 24 weeks post randomization. Secondary outcome between-group differences were assessed using analysis of covariance (ANCOVA), with change from randomization as the dependent variable, treatment and pooled site as the independent variables, and randomization value as covariate. Within-group differences were analyzed using one-way ANOVA.

Poisson regression was planned for the analysis of the annualized rates for hypoglycemia; however, due to over dispersion, the analysis was performed using negative binomial regression.

The study design was approved by academic ethics review boards across Canada, including The University of Western Ontario. All patients provided written, informed consent.

RESULTS

Site Investigator Characteristics

Forty-seven physician sites participated in the START trial. Physicians were predominately male (87.8%), had a mean age of 53.5 years (SD=8.02), and had been practicing for 26 years (SD=8.6). Most practiced primary care medicine (90%) in an urban setting (75%), had access to allied health staff (75.6%), and had an average of >150 patients with diabetes (80.5%).

Study Population

At the end of the run-in phase 49% of patients (316/641) were randomized. Figure 1 outlines the disposition of patients including 170/641 patients who did not meet randomization requirements but were followed. The dropout rate was 6.5% (10/154) and 11% (18/162) for the patient-managed and physician-managed groups respectively.

Patient baseline demographics and clinical characteristics were comparable between intervention

groups (Table 1). Patients were predominantly male (60.8%) with a mean age of 60.4 years. Median follow-up was 168 days for both the patient managed arm and physician-managed arms.

Primary outcome

After a mean (SD) follow-up of 159.4 days (36.2), the primary outcome was achieved by 28.4% of subjects in the patient-managed arm and 21.2% in the physician-managed arm, an absolute difference of 7.2% (95% CI: -3.2 to 17.7). The lower end of the 95% CI for the difference, -3.2, was within the predefined non-inferiority boundary (set at $\geq -5.0\%$), demonstrating non-inferiority ($p=0.0105$) of the patient-managed group.

Secondary outcomes

Glycemic Control

Over the course of the study (randomization to end of treatment), HbA_{1C}, the change between FPG and 2hr PPG and the total area under the 7-point glucose profile curve, decreased significantly for both the patient-managed and physician-managed groups. No statistically significant differences between the titration algorithms were evident (Table 2).

There was a significant increase in FPG in both the patient-managed and physician-managed, with no significant difference between algorithms (Table 2).

Medication Dose

Glargine dose did not significantly increase within or between groups after the run-in-phase: mean units at randomization, 12 weeks and 24 weeks were 59.2 U, 58.1 U and 59.8 U respectively for the patient-managed group and 53.1 U, 53.6 U and 53.0 U respectively for the provider-managed group.

Following randomization, mean glulisine dose significantly increased for patients in both groups ($p=0.0001$). The patient-managed group increased from $2.0 \text{ U} \pm 0.47$ to $16.3 \text{ U} \pm 17.57$ and the physician-managed group from $2.5 \text{ U} \pm 1.11$ to $12.0 \text{ U} \pm 11.29$. This increase was significantly higher by the end of treatment for patient-managed patients with an adjusted mean difference (SE) of 5.6 (1.77) (95% CI [2.1 to 9.1], $p=0.0018$).

Quality of Life

No significant differences in quality of life were evident between groups as assessed by patient's total satisfaction score and perceived hyper/hypoglycemia. Patients ranked their mean satisfaction as "high" (out of 18) by the end of their treatment (patient-managed: 13.39 ± 5.32 and physician-managed: 13.26 ± 5.90).

Resource Utilization

There were no between group differences in the number of blood glucose testing strips used and

visits to a healthcare professional. The number of telephone calls made to the physician's office were significantly lower for patients managing their own treatment, with an adjusted mean difference (SE) of -0.74 calls (0.20) (95% CI -1.14 to -0.35; $p=0.0001$).

Body Weight

Mean body weight significantly increased ($p<0.001$) from randomization to end of treatment for both the patient-managed (98.54 ± 21.15 kg to 100.56 ± 21.68 kg) and physician-managed (99.09 ± 22.86 kg to 100.23 ± 23.50 kg) groups. Between-group analysis showed a significantly higher increase at end of treatment for the patient-managed group, with an adjusted mean difference (SE) of 0.87 (0.44) (95% CI [0.00 to 1.73], $p=0.0494$).

Safety -Hypoglycemia

There was no difference between the groups for the proportion of patients who experienced a minimum of one hypoglycemic event (Table 3). Annualized symptomatic hypoglycemic events were 7.1 confirmed events per person per year in the patient-managed group and 6.2 in the physician-managed group ($p=0.5074$). The annualized rates for only those patients with at least one confirmed hypoglycemic event were 11.1 and 10.4 were not significantly different ($p=0.6531$). The majority of hypoglycemic events, 58.3% and 62.7% for the patient-managed and physician-managed groups respectively, occurred between 6 am and noon.

Physician Satisfaction

Forty-one physicians responded to the satisfaction survey (return rate=87%) with a mean satisfaction score of 14.0 ± 7.21 , range: -6 to 21. By the end of the trial, the majority of physicians (61%) reported a very high level of confidence initiating and intensifying insulin therapy.

CONCLUSIONS

This large, prospective, multicenter RCT demonstrated that similar glycemia control can be achieved by patients using a simple breakfast preprandial insulin titration approach when compared to a physician managed strategy. The self-titration intervention was designed to capitalize on the common practice that most patients on a basal insulin routinely test their blood glucose in the morning (6) and the addition of a breakfast prandial insulin self-titration algorithm requires only one extra self-monitoring test later in the same morning hence maximizing patient convenience. In addition, the START study was carried out in primary care practices highlighting the feasibility of an insulin intensification strategy in this setting.

In the START study patients responsible for managing their insulin titration were more aggressive at titrating glulisine when compared to the physician-managed group (16.3 U vs 12 U; $p=0.0018$). In addition, the START modified basal-bolus strategy significantly improved HbA1c levels for both groups. All improved despite rising FPGs following randomization when, by

protocol, the dose of basal insulin was fixed. This highlights the relative contribution of breakfast PPG to overall control.

Furthermore, patients were satisfied with their treatment despite increases in body weight and at least one confirmed hypoglycemic episode occurring in the majority (63.6% and 58.6%) of patients. The proportion of episodes defined in START as < 3.1 mmol/L (55.8 mg/dL), were 33.8% and 30.9% similar to Lankisch who reported 34.2% when defined as < 3.3 mmol/L (59.4 mg/dL).(22)

These findings build on other studies comparing patient and physician insulin titration approaches. Selam and Meneghini (26) compared a patient algorithm versus standard care physician adjustment of basal insulin for patients on basal-bolus insulin therapy. Patients using the algorithm increased their dose to a significantly greater extent and achieved significantly greater reductions in FBG. There were no significant differences in the patient versus physician titration for reduction in HbA_{1C}, or the rate of hypoglycemic events. Davies et al.(7) compared patient and physician titrated basal insulin algorithms for patients sub-optimally controlled and found no significant difference in the rate of severe hypoglycemia, however the physician titrated group had significantly lower overall incidence of hypoglycemia. The patient titration group resulted in significantly increased dose of basal insulin and greater reduction in HbA_{1C} and FBG. Combined with the results of the START trial, these studies demonstrate that patients can

successfully titrate both basal and bolus insulin.

Studies have identified that patients in the primary care setting often fail to achieve optimal targets due to clinical inertia involving insulin titration.(3) A stepwise approach recommended by Racciah et. al. (24) may help to overcome patient (27-29) and physician (27, 30) barriers to the initiation and titration of insulin. The START study utilized an empowerment approach (31) to patient care by supporting patients to make autonomous, informed decisions about their diabetes self-management. Patient understanding and involvement in their treatment (24)and a collaborative relationship between the physician and patient is important to improve compliance and achieving glycemic goals.(32, 33)

This study also highlights the need for a basal-plus strategy for patients similar to these study patients within a primary care practice, because 56% (315/561) of patients prescribed basal insulin required prandial insulin intensification after the 12 week run-in phase. This is consistent with 30-50% reported elsewhere.(24) In addition, for those who do initially achieve target on basal insulin alone, approximately 25% will eventually require bolus insulin.(34) As only 21 and 28% of patients in this trial achieved optimal control with no severe hypoglycemia highlights the fact that additional bolus therapy at other meals may be required.

Limitations

The START study was an open-label trial, and both physicians and patients were aware of the

patient's randomization status and may have co-intervened in unmeasured ways depending on their biases regarding patient versus physician-directed insulin titration.

The glargine dose at randomization was maintained and may have diminished the opportunity for optimal glycemic control but as this protocol occurred for both groups it affected both groups equally and was unlikely to affect the primary outcome. Nevertheless, this study provides preliminary data to demonstrate the feasibility and safety of implementing insulin intensification in a primary care clinical environment.

In summary, the START study results offer a potential strategy to mitigate clinical inertia involving insulin intensification in the primary care setting and resulted in an overall improvement in glycemic control. A patient-driven algorithm for basal insulin plus bolus insulin at breakfast is a simple, safe and effective strategy to improve glycemic outcomes without severe hypoglycaemia in the primary care environment.

AUTHOR CONTRIBUTIONS

The authors contributed as follows: SBH, JFY, LB, JS, BA, HG: Contributed to the design of the trial, overview of its execution, and reviewed and edited the manuscript. In addition: JS supervised statistical analysis; SBH and SWB wrote the manuscript.

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Disclosures

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FIGURE LEGENDS

Figure 1: Disposition of Patients

TABLES

Table 1: Patient baseline demographics and clinical characteristics by titration algorithm, all randomized patients (n=316)

Demographics and characteristics	Patient- managed N=154	Physician- managed N=162	<i>p</i> value
Age, years (SD)	60.4 (10.0)	60.2 (9.8)	0.72
Male, n (%)	90 (58.4)	102 (63.0)	0.50
Ethnicity – Caucasian, n (%)	142 (92.2)	137 (84.6)	0.04
Body mass index, kg/m ² (SD)	34.1 (7.2)	34.3 (7.9)	0.74
Duration of diabetes, years (SD)	12.1 (8.0)	12.2 (8.6)	0.86
HbA _{1c} at randomization, % (SD)	8.2 (0.8)	8.3 (1.3)	0.86
mmol/mol (SD)	66 (8.7)	67 (14.2)	
Insulin-naïve patients, n (%)	75 (48.7)	81 (50.0)	0.94
OR			
Patients on basal insulin at screening, n (%)	79 (51.3)	81 (50.1)	
Duration of basal insulin therapy, years (SD)	2.2 (3.4)	2.5 (2.7)	0.42
Patients on oral anti-hyperglycemic medications at screening, n (%)	149 (96.8)	159 (98.1)	0.49
Duration of OADs, years (SD)	8.4 (6.6)	8.5 (6.8)	0.93
OADs at screening, n (SD)	2.1 (0.7)	2.0 (0.7)	0.47
Patients with diabetes-related complications at screening n, (%)	47 (30.5)	57 (35.2)	0.38
Nephropathy n (%)	21 (13.6)	24 (14.8)	0.76
Retinopathy, n (%)	15 (9.7)	12 (7.4)	0.46
Foot ulcers, n (%)	3 (1.9)	4 (2.5)	0.75
Neuropathy, n (%)	19 (12.3)	39 (24.1)	0.01
Cardiovascular disease, n (%)	37 (24.0)	37 (22.8)	0.80
Cerebrovascular disease, n (%)	5 (3.2)	9 (5.6)	0.32
Peripheral vascular disease, n (%)	4 (2.6)	5 (3.1)	0.79

Table 2: Within and between-group change from randomization to end of treatment for glycemic control, modified intent-to-treat patients

Glycemic Control	Group	Descriptive Statistics Mean (SD)		Change at end of treatment Within group P value	Change at End of Treatment: Between Groups†	
		Randomization	End of Treatment		95% CI	Between- group P-value§
HbA _{1C} * % mmol/mol	PM** (N=154)	8.2 (0.8) 66 (8.3)	7.7 (0.9) 60 (9.5)	0.0001	-0.27 to 0.13	0.49
	HCPM*** (N=159)	8.3 (1.06) 67 (11.6)	7.8 (1.2) 62 (13.3)	0.0001		
Difference between FPG† and 2HrPPG‡ mmol/L	PM (N=121)#	3.7 (2.7)	1.4 (3.0)	0.0001	-1.13 to 0.49	0.43
	HCPM (N=129)	4.4 (3.2)	1.8 (3.2)	0.0001		
FPG mmol/L mg/dL	PM (N=121)	6.2 (2.1) 112.1 (37.1)	6.8 (2.2) 122.0 (39.2)	0.039	-0.33 to 0.76	0.44
	HCPM (N=129)	6.0 (1.7) 108.4 (31.0)	6.6 (2.1) 119 (38.5)	0.0097		
Total area under 7-point glucose profile mmol/L*hour	PM (N=121)	215.2 (40.7)	202.9 (40.0)	0.0045	-10.42 to 9.60	0.94
	HCPM (N=129)	225.6 (49.8)	206.0 (44.8)	0.0001		

*HbA_{1C} – glycated hemoglobin; ** PM – patient managed, *** HCPM – healthcare professional managed

†FPG – fasting plasma glucose

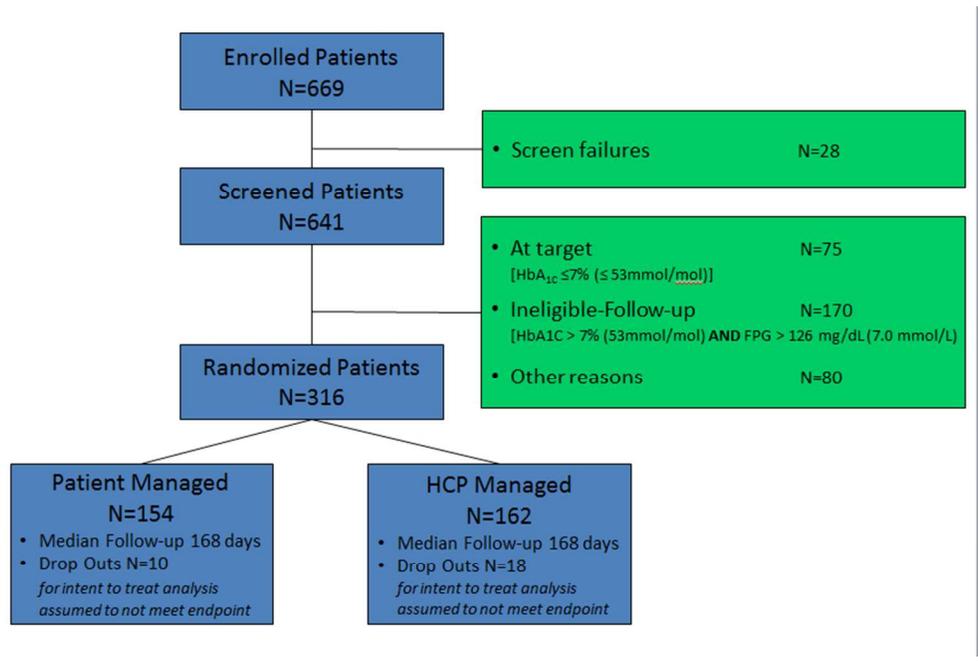
‡2HrPPG – 2 hour postprandial glucose (after breakfast)

33 patients in the PM and 30 patients in the HCPM groups did not provide 7 point glucose readings

§These are *between-group* results where change from randomization to end of treatment was compared between PM and HCPM groups using ANCOVA. Change from randomization was the dependant variable with treatment and pooled site as the classified independent variables, and randomization value as covariate

Table 3:
Hypoglycemia event rates by titration algorithm

Type of symptomatic hypoglycemic episodes	Patient Managed (N=154)	HCP Managed (N=162)	Between Group Difference 95% CI	P-Value
Percentage of Patients with at least one Symptomatic Hypoglycemic Episode				
All hypoglycemic episodes	67.5%	61.1%	-17.0, 4.1	0.23
All confirmed hypoglycemic episodes	63.6%	58.6%	-15.7, 5.7	0.36
Episodes at <3.1mmol/L (55.8 mg/dL)	33.8%	30.9%	-13.2, 7.4	0.58
Nocturnal	26.0%	28.4%	-7.4, 12.2	0.63
Severe	1.9%	1.9%	-3.1, 2.9	0.95
Annualized Episode Rate: Based on negative binomial regression				
All hypoglycemic episodes	8.9	8.1	0.62, 1.32	0.61
All confirmed hypoglycemic episodes	7.1	6.2	0.60, 1.29	0.51
Episodes at <3.1 mmol/L (55.8 mg/dL)	1.4	3.6	0.45, 1.25	0.27
Nocturnal	0.9	0.8	0.53, 1.58	0.75
Severe	0.02	0.03	0.24, 9.32	0.68
Annualized Episode Rate for Patients Having at Least One Event): Based on negative binomial regression				
	Patient Managed (N=104)	HCP Managed (N=99)		
All hypoglycemic episodes	13.2	13.0	0.76, 1.28	0.93
All confirmed hypoglycemic episodes	11.1	10.4	0.71, 1.24	0.65
Episodes at <3.1 mmol/L (55.8 mg/dL)	2.9	2.3	0.52, 1.26	0.34
Nocturnal	3.5	2.9	0.58, 1.15	0.25
Severe	1.3	1.7	0.32, 5.62	0.69



Disposition of Patients
307x200mm (72 x 72 DPI)

HCP SATISFACTION QUESTIONNAIRE

Date Completed ___/___/___ (day/month/year)

*Please answer each question by circling a number on each of the scales to indicate the extent to which you agree with each**statement. If you neither agree nor disagree, circle "0".***1. I found basal plus treatment strategy as a simple method to implement in my day to day activity for the management of T2DM.**

Totally agree 3 2 1 0 -1 -2 -3 Totally disagree

2. I found basal plus treatment strategy effective in the management of T2DM.

Totally agree 3 2 1 0 -1 -2 -3 Totally disagree

3. The patient-managed titration algorithm is simple and easy to follow for my patients.

Totally agree 3 2 1 0 -1 -2 -3 Totally disagree

4. I am satisfied with the clinical outcome of my patients using the patient-managed titration algorithm.

Totally agree 3 2 1 0 -1 -2 -3 Totally disagree

5. The experience I acquired with the patient-managed titration algorithm helped increase/reinforce my belief that patients can actively participate in their disease management.

Totally agree 3 2 1 0 -1 -2 -3 Totally disagree

6. I would use the START study patient-managed titration algorithm in my daily clinical practice.

Totally agree 3 2 1 0 -1 -2 -3 Totally disagree

7. I would recommend the START study patient-managed titration algorithm to my peers.

Totally agree 3 2 1 0 -1 -2 -3 Totally disagree