

Role of Mobile Technology to Improve Diabetes Care in Adults with Type 1 Diabetes: The Remote-T1D Study iBGStar[®] in Type 1 Diabetes Management

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ABSTRACT

Introduction: The role of mobile technology in patient-reported outcomes (PRO) and glycemic control in adults with type 1 diabetes (T1D) needs further evaluation.

Methods: The single-center, prospective, 6-month, open-label, investigator-initiated study randomized 100 subjects with T1D in a 1:1 fashion to a control group using self-monitoring of blood glucose (SMBG) with Accu-Chek Nano[®] and an intervention group using SMBG with iPhone plus glucose meter (iBGStar[®]). The primary endpoint was the change in PRO (hypoglycemia fear score, behavior and worry subscores). Secondary outcomes were the

improvement in glycemic variability indices and the reduction in A1c values.

Results: Baseline demographics and glycosylated hemoglobin (A1c) values were similar in the two groups. There was a significant decrease in A1c value at 6 months in iBGStar[®] group compared to the control group (-0.16 vs. -0.51 , $p = 0.04$). The total insulin dose increased significantly in the iBGStar[®] group at 3 months but did not change at 6 months. The hypoglycemia fear scale (PRO) improved in both groups at 6 months (-1.4 ± 10.0 vs. -3.9 ± 12.5 , $p = 0.32$).

Conclusion: The use of iBGStar[®] resulted in better glycemic control and improvement in some PRO (hypoglycemia fear and behavior scores) compared to the control group at 6 months with no increased risk of hypoglycemia.

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Keywords: Continuous glucose monitoring; Diabetes; Glucometer; Hypoglycemia; iBGStar; iPhone; Mobile technology; Self-monitoring of blood glucose; Type 1 diabetes

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INTRODUCTION

With increasing incidence of type 1 diabetes (T1D) by 2–5% annually, 5 million people are

estimated to have T1D by 2050 in the USA [1, 2]. Though intensive insulin therapy (IIT) has been shown to reduce the risk of micro- and macrovascular complications of diabetes, it is associated with a significant increase in the risk for severe hypoglycemia [3]. Even fear of hypoglycemia itself poses a significant psychological factor in patients with T1D, preventing them from achieving good glycemic control [4]. Despite increases in diabetes care, less than 20% of patients with T1D achieve good glycemic control [as defined by a glycosylated hemoglobin (A1c) of less than 7%] [5].

Self-monitoring of blood glucose (SMBG) is a valuable tool for decision-making for both patients and clinicians. Frequent SMBG has been shown to improve A1c and reduce hypoglycemia and hypoglycemia fear in patients with type 1 diabetes [6, 7]. The American Diabetes Association (ADA) recommends that patients whose medication regimen includes multiple daily insulin injections or insulin pumps should test their blood glucose three times or more per day [8]. However, not all patients with diabetes test blood glucose three times or more a day [5]. Hurdles in poor adherence to SMBG include (a) inaccurate meters, (b) big and bulkier devices, (c) need to poke a finger multiple times, (d) need to carry an additional device all the time, and (e) paper log book entry [6, 7, 9, 10]. These difficulties result in poor compliance and inadequate glucose control with wide glucose excursions.

The ubiquity of smartphones and increasing availability of diabetes management mobile applications present a potential method to reduce the daily time and effort required to perform SMBG tasks and share data with a healthcare provider. Small studies have shown improvement in glycemic control with the use of electronic log book and Internet-based glucose monitoring systems [11]. However, these studies are limited by small sample size and short duration and no reporting of hypoglycemic events [11]. Using mobile technology to facilitate the review of blood glucose data by both patients and providers could provide an opportunity to reduce glycemic variability and its associated complications [12]. The iBGStar[®] system is a blood glucose meter that attaches to

an iPhone as a peripheral device. Using the iBGStar[®] with the Diabetes Manager App, a user's iPhone can function as a glucometer. The Diabetes Manager App takes advantage of the existing user interface and communication capabilities of the iPhone to provide IMBG functionality on a mobile device. This study examined the effect of iBGStar[®] in combination with Diabetes Manager mobile application on patient-reported outcomes (PRO) and glycemic control in adults with T1D.

METHODS

Patient Selection

This study was a single-center, prospective, randomized, open-label, and conducted at the Barbara Davis Center for Diabetes. The protocol was approved by Colorado Multiple Institutional Review Board at the University of Colorado. Adults (≥ 18 years) with T1D of more than 1-year duration and A1c below 10% were enrolled. Pregnant women and those who intended to conceive during the study period were excluded. Participants with T1D on systemic or inhaled steroids, history of severe hypoglycemia in the last 6 months, history of anemia or hemoglobinopathies, history of pancreatitis, history of skin disease, or allergy to adhesives and bandages precluding continuous glucose monitor (CGM) use were also excluded from the study.

Study Design, Treatment, and Follow-Up

Subjects were randomized on a 1:1 basis to either the control group or intervention group using stratified block randomization based on a screening A1c < 8.5 or ≥ 8.5 to reduce the possibility of sampling error and ensure that randomization resulted in similar A1c results in each group. The control group were provided with Accu-Chek Nano[®] meters and trained on their use at baseline and reinforced at week 1. The iBGStar[®], an iPhone 4 or 4S, and the Diabetes Manager App were provided to the intervention group. All subjects were provided with a

Dexcom SEVEN Plus[®] blinded CGM sensor. The provider maintained contact with the subjects by electronic communication (email, text, or phone) every 7–14 days during the study. Subjects in the control group were encouraged to contact their provider as needed by traditional communication (email, fax, or phone). Those in the intervention group were invited to contact the research site if their blood glucose reading was below 60 or above 300 mg/dL using the Diabetes Manager App, which sends a notification text from the iPhone to the provider. All diabetes treatment decisions were based on SMBG readings from either the iBGStar[®] or Accu-Chek Nano[®] glucometer, depending on group assignment. Subjects were trained to use glucose log books and instructed to check blood glucose at least three times per day during the study.

All subjects had similar clinic and phone visits for 3 months, with a 3-month extension. A total of eight visits were required—a screening visit, four in-clinic visits, and three phone calls. A Dexcom SEVEN Plus[®] blinded CGM sensor was inserted each clinic visit starting from visit 2 for a total of four visits (for four separate 7-day periods of blinded CGM at visits 2, 4, 6, and 8). During the week of blinded CGM use, subjects were not allowed to use their own real-time CGMs. Subjects were instructed not to take acetaminophen during blinded CGM period as per the label.

All the participants were trained on glucose diaries and were asked to check blood glucose at least three times a day during the study period. All diabetes treatment decisions were based on SMBG readings from iBGStar[®] in the intervention group and Accu-Chek Nano[®] glucose meter in the control group. The study design and visits are shown in Fig. 1. All participants completed the study and attended to all visits.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all participants for being included in the study.

Outcome Measurements

A1C, complete metabolic panel, and complete cell counts were measured at baseline, 1, 3, and 6 months. A1c was measured by DCA 2000. Data on insulin dose was collected from participants by self-report based on logbook entries. The PRO directly describes the patient's perception of a disease and its treatment without the interpretation of responses by a physician. Hypoglycemia perspective questionnaire and hypoglycemia fear score are the most common tools used for hypoglycemia assessment. Hypoglycemia fear was measured using a 27-question instrument (score range 27–135) with subscales for behavior (10 questions) and worry (17 questions) at the screening and 3- and 6-month visits [13] (Supplement 1). Measurements of average blood glucose and glucose variability were carried out from blinded CGM tracings.

Statistical Analysis

The analysis was conducted with the intent-to-treat concept. The primary efficacy endpoint was patient-reported outcomes, including the change in the hypoglycemia fear questionnaire score from baseline to 3 and 6 months. Secondary outcomes were the improvement in glycemic variability indices and the reduction in A1c values. Improvement in glycemic control was measured as the difference in the change in A1c laboratory values of the two arms of the study between baseline and 3 and 6 months. Changes in the primary and secondary efficacy endpoints were assessed using paired *t* tests examining changes from baseline to 3 months and baseline to 6 months. Linear regression mixed models were used to assess changes in the primary and secondary endpoints over time, using repeated measures analyses. As this was a pilot study, formal power calculations were not performed for the primary or secondary endpoints. Statistical significance was defined as $p < 0.05$. All analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC, USA).

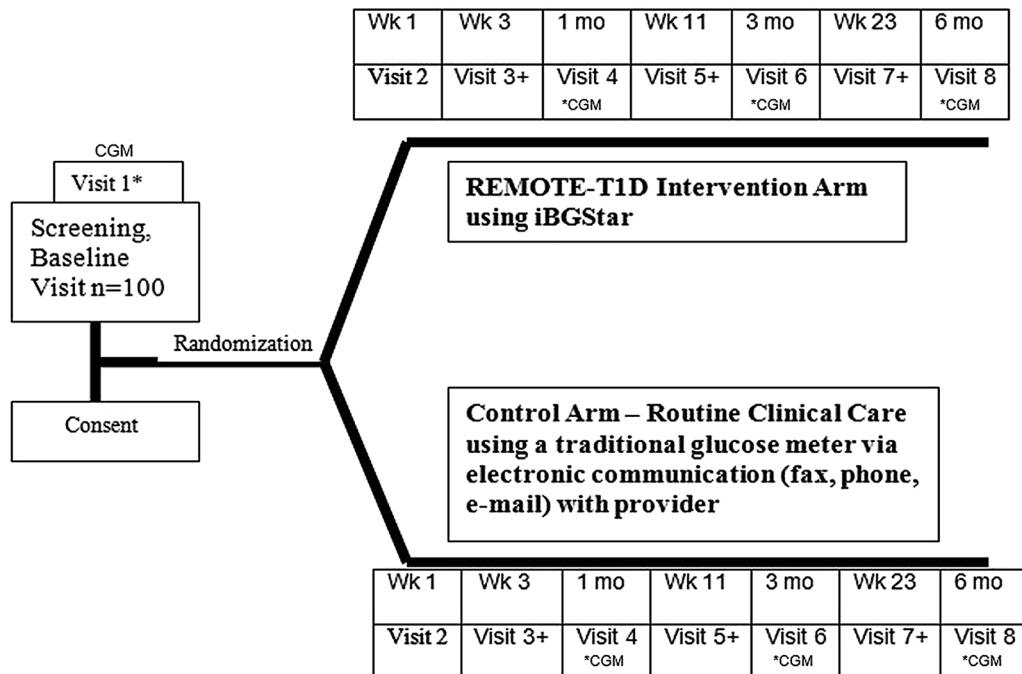


Fig. 1 Study design. Asterisk CGM blinded insertions 7 days prior to visit, plus sign phone visit

RESULTS

Fifty participants with T1D were randomized to the intervention arm (iBGStar[®]), and an equal number of participants were randomized to the control group (Accu-Chek Nano[®]). The mean age, duration of diabetes, body mass index (BMI), A1c level, the number of self-monitored blood glucose (SMBG) measures, daily insulin basal and bolus dose, and total daily insulin dose per day were similar between control and intervention groups (Table 1). Similarly, there was no difference in hypoglycemia fear scale, behavior scale, and worry scale between the control and intervention groups at baseline (Table 1).

As shown in Table 2, there were decreases in the overall hypoglycemia fear score in both groups after 3 months, but these decreases were no longer significant at 6 months. There was no difference in the magnitude of the changes in hypoglycemia fear in the study group at either 3 or 6 months. When examined by subscore, hypoglycemia fear behavior score decreased in only the iBGStar[®] group at 3 months, but this change did not persist at 6 months. The

hypoglycemia fear worry score declined in both groups at 3 months and remained significantly reduced only in the control group at 6 months. However, the changes in scores for both subscales did not differ by the study group. The total insulin dose increased significantly in the iBGStar[®] group at 3 months but did not change at 6 months. There was no statistically significant difference between iBGStar[®] and control groups regarding the number of hypoglycemic events and the average number of SMBG/day.

There was a decrease in A1c among both the control and iBGStar[®] groups at 3 months, although the amount of change in A1c was not different between groups (−0.21 vs. −0.4, $p = 0.20$) (Fig. 2). However, at 6 months, there was a significant decrease in A1c from baseline only in the iBGStar[®] group, and the amount of change was significantly greater in the iBGStar[®] group than in the control group (−0.16 vs. −0.51, $p = 0.04$) (Fig. 2). The percentage of time spent in hypoglycemia (<70 mg/dl) did not differ by study group (Fig. 3). There was no BMI change at 3 and 6 months in groups.

In addition to the univariate analyses, linear mixed modeling was used to examine the

Table 1 Baseline characteristics of the study participants ($n = 100$)

	iBGStar ($n = 50$)	Controls ($n = 50$)	p value
Age (years)	38 ± 11	39 ± 12	0.79
Diabetes duration (years)	25 ± 12	22 ± 13	0.24
Gender (% male)	48	56	0.4
BMI (kg/m^2)	27.1 ± 5.1	27.3 ± 5.5	0.82
A1c (%)	8.0 ± 0.9	7.7 ± 1.0	0.15
Number of SMBG measures per day	4.8 ± 1.1	5.2 ± 1.1	0.07
Basal insulin dose per day	31 ± 13	27 ± 17	0.20
Bolus insulin dose per day	22 ± 15	26 ± 18	0.19
Total insulin dose per day	53 ± 20	53 ± 29	0.93
Total insulin per day per kg of body weight	0.7 ± 0.2	0.7 ± 0.3	0.88
Hypoglycemia fear scale	59 ± 12	58 ± 13	0.70
Behavior scale	24 ± 6	23 ± 6	0.32
Worry scale	35 ± 9	35 ± 10	0.93

change in primary and secondary endpoints over the three study visits using a repeated measures analysis. Hypoglycemia fear score was examined, adjusting for group, age, diabetes duration, sex, BMI, daily insulin dose per kilogram body weight, and A1c. There remained no significant differences by group either overall ($p = 0.77$) or across visits ($p = 0.55$), but hypoglycemia fear score was significantly lower in men than in women (estimate -5.9 , $p = 0.046$) and was negatively associated with insulin dose (estimate -6.2 , $p = 0.04$). Hypoglycemia fear score was not associated with age ($p = 0.88$), diabetes duration ($p = 0.50$), BMI ($p = 0.68$), or A1c ($p = 0.41$) (Table 3).

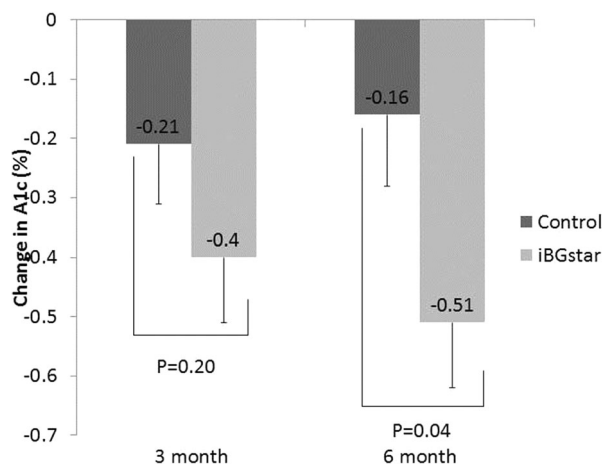
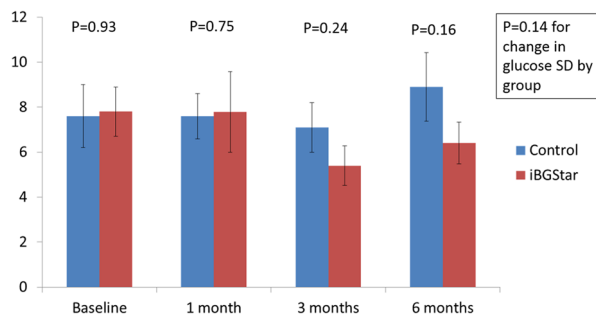
Table 2 Change in hypoglycemia fear scores, insulin doses, and SMBGs by group over 3 and 6 months

	iBGStar ($n = 50$)	Control ($n = 50$)	p value
Hypoglycemia fear score			
Change 3 months	$-4.5 \pm 9.4^*$	$-4.2 \pm 12.2^*$	0.90
Change 6 months	-1.37 ± 9.9	-3.9 ± 12.5	0.32
Hypoglycemia behavior subscore			
Change 3 months	$-2.5 \pm 6.1^*$	-1.2 ± 6.0	0.32
Change 6 months	-0.10 ± 5.2	-0.29 ± 6.3	0.88
Hypoglycemia worry subscore			
Change 3 months	$-2.0 \pm 6.3^*$	$-3.0 \pm 9.1^*$	0.55
Change 6 months	-1.27 ± 7.5	$-3.6 \pm 9.7^*$	0.23
Total insulin dose (units/day)			
Change 3 months	$7.7 \pm 20.9^*$	1.7 ± 18.3	0.16
Change 6 months	5.0 ± 16.9	1.1 ± 15.0	0.27
Basal insulin dose (units/day)			
Change 3 months	1.7 ± 9.3	$2.5 \pm 7.6^*$	0.68
Change 6 months	2.7 ± 11.8	1.4 ± 8.5	0.55
Bolus insulin dose (units/day)			
Change 3 months	6.0 ± 21.0	-0.7 ± 16.0	0.09
Change 6 months	2.3 ± 15.0	-0.3 ± 13.6	0.42
Average number of SMBGs/day			
Change 3 months	$-0.3 \pm 0.7^*$	$-0.5 \pm 0.9^*$	0.24

Table 2 continued

	iBGStar (<i>n</i> = 50)	Control (<i>n</i> = 50)	<i>p</i> value
Change 6 months	-0.3 ± 0.9	-0.4 ± 0.9*	0.48
Number of hypoglycemic events			
At 3 months	11.0 ± 14.2	13.7 ± 15.6	0.40
At 6 months	21.5 ± 15.5	25.5 ± 31.0	0.48

* From baseline: $p < 0.05$

**Fig. 2** Change in A1c by study group at 3 and 6 months**Fig. 3** Percentage of time spent hypoglycemic (<70 mg/dl) by group over 6 months

Similarly, linear mixed modeling was used to examine change in A1c across the three visits, adjusted for group, age, diabetes duration, sex, BMI, and daily insulin dose per kilogram body weight. In this model, there remained no

Table 3 Hypoglycemia fear predicted by group

Effect	Num DF	Den DF	<i>F</i> value	Pr > <i>F</i>
Visit	2	95	3.26	0.0425
Group	1	95	0.09	0.7659
Age	1	95	0.02	0.8816
Duration	1	95	0.45	0.5039
Sex	1	95	4.08	0.0461
BMI	1	95	0.17	0.6815
A1c	1	95	0.68	0.4116
Insulin dose per kg	1	95	4.35	0.0396
Visit × group	2	95	0.61	0.5447

Hypoglycemia fear predicted by group, adjusted for age, duration, and sex, plus BMI, A1c, and insulin dose

significant difference by study group either overall ($p = 0.60$) or across visits ($p = 0.14$), although the change in A1c was significantly associated with insulin dose (estimate 0.5193, $p = 0.02$). There was no association between A1c across study visits and age ($p = 0.22$), diabetes duration ($p = 0.76$), sex ($p = 0.21$), or BMI ($p = 0.76$) (Table 4).

In a post-study survey, 88% of the subjects who used iBGStar® were satisfied with the system. Seventy-five percent of the subjects found the iBGStar® system with the Diabetes Manager App on the iPhone easier than their conventional glucometer for managing their diabetes. Diabetes Manager App was found to be very user-friendly by about 90% of the subjects.

DISCUSSION

Blood glucose monitoring is an important part of diabetes management, especially in patients on insulin. The Diabetes Control and Complications Trial showed that frequent blood glucose monitoring along with intensive therapy is required to maintain tight glycemic control [14].

Communication errors between the patients and the providers, absence of documentation of

Table 4 A1c prediction by group

Effect	Num DF	Den DF	F value	Pr > F
Visit	2	95	12.85	<0.0001
Group	1	95	0.28	0.5959
Age	1	95	1.56	0.2153
Duration	1	95	0.10	0.7554
Sex	1	95	1.57	0.2132
BMI	1	95	0.10	0.7564
Insulin dose per kg	1	95	4.99	0.0278
Visit*Group	2	95	2.04	0.1357

A1c predicted by group, adjusted for age, duration and sex, plus BMI and insulin dose

blood glucose results, and failure of downloading glucometers in care centers are common difficulties in diabetes care. New technologies require a better understanding by both patients and healthcare workers [15]. An accurate and convenient way for routine blood glucose monitoring and reporting is essential for following the treatment and making necessary therapeutic changes. Integration of smartphones into our life brought new opportunities in healthcare. The use of the Diabetes Manager App with the iBGStar[®] facilitated electronic communication between participants and providers. The precision of iBGStar[®] was shown previously in an in vitro diagnostic device study [16]. Diabetes Manager App allowed participants to upload and review SMBG data on an iPhone. Even though there was no significant difference between hypoglycemia fear or behavior scales, the subjects indicated that they felt more comfortable using the iBGStar[®] system. Ease of use and convenience probably resulted in greater patient satisfaction at the post-study survey. The app allowed the patient to filter and dynamically interact with log book data, graph trends, and view statistics. Rather than searching through a report, the user can take advantage of features in the app to produce specific queries related to their needs.

In our study, using the iBGStar[®] system improved A1c at 3 months which was maintained at 6 months when compared to the control group. Increased insulin requirements may partially explain the decrease of A1C in the iBGStar[®] group.

This was a pilot study. One of the strengths of this study was that no one had previously evaluated the role of mobile technology in diabetes care. Our goal was to learn from this study and plan for a much larger study using social media in the future after implementing changes that would be learned from this pilot study. We had objective measures of patient-reported outcomes and treatment satisfaction using validated tools.

Limitations of this study were that this was a short-term (6 months) study in a single center and we only focused on hypoglycemia risk at CGM and we did not analyze the other blood glucose variabilities. Therefore, the results may not be generalized.

CONCLUSIONS

The use of iBGStar[®] in combination with Diabetes Manager mobile application improved some PRO (hypoglycemia fear and behavior score) and glycemic control at 6 months without an increased risk of hypoglycemia. Further studies would be required to determine the effects of iBGStar[®] system and Diabetes Manager App in the long term.

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Compliance with Ethics Guidelines. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all participants for being included in the study. The protocol was approved by Colorado Multiple Institutional Review Board at the University of Colorado, Aurora, CO, USA.

Data Availability. All data generated or analyzed during this study are included in this published article/as supplementary information files.

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